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EFFECTS OF SMOKING CESSATION ON SEXUAL HEALTH IN MEN

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EFFECTS OF SMOKING CESSATION ON SEXUAL HEALTH IN MEN

by

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DEDICATION

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Effects of Smoking Cessation on Sexual Health in Men

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Cigarette smoking represents the most preventable cause of morbidity and mortality in the world today, and is responsible for enormous health-related economic burdens. Among other medical sequelae, erectile impairment has been shown to be associated with chronic tobacco use. The primary aim of the present study was to provide the first empirical investigation of the effects of smoking cessation on physiological and subjective indices of sexual health. Sixty-five long-term, heavy smoking men participated in a smoking cessation program and were assessed at baseline (while smoking regularly), at mid-treatment (while using a high dose nicotine transdermal patch), and at 4-week follow-up. Physiological and subjective sexual arousal indices, as well as self-reported sexual functioning (as measured by the International Index of Erectile Functioning (IIEF)) were assessed during each visit. Intent-to-treat analyses indicated that at follow-up successful quitters (n = 20), compared to those who relapsed (n = 45), showed significant improvements in physiological and subjective sexual arousal. Specifically, men demonstrated enhanced erectile responses, decreased latencies to reach maximum erectile capacity, and faster onset to reach maximum subjective sexual arousal. Although participants displayed across-session enhancements in self-reported sexual function,

successful quitters did not show a differential improvement compared to participants who relapsed. The results of the present investigation provide the first empirical evidence that smoking cessation significantly enhances both physiological and self-reported indices of sexual health in long-term male smokers, irrespective of baseline erectile impairment. It is hoped that these results may serve as a novel and enticing means to influence men to quit smoking. Increasing successful smoking cessation in men would significantly enhance quality of life, substantially reduce premature death, and alleviate enormous economic burdens caused by smoking-related diseases.

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CHAPTER 1: INTRODUCTION

1.1 Tobacco use: Prevalence and public health

Tobacco use constitutes the single most preventable cause of disease and death in the world today (Centers for Disease Control and Prevention, 2002), and introduces a wide range of diseases such as cardiovascular diseases (e.g., coronary heart disease, peripheral vascular disease, hypertension, stroke (Fielding, Husten, & Eriksen, 1998)), respiratory diseases (Fagerström, 2002), and many types of cancer (U.S. Department of Health and Human Services, 2004). These smoking-related diseases reduce quality of life and shorten quantity of life by approximately 10 years (Doll, Peto, Boreham, & Sutherland, 2004). Each year, smoking is responsible for the deaths of over 269,000 men and 173,000 women in the United States (Centers for Disease Control and Prevention, 2008b) and approximately 5 million premature deaths annually worldwide (Global Youth Tobacco Survey Collaborative Group, 2003). In fact, in the United States one in every five deaths is smoking related, which translates to an estimated $97 billion in health-related economic losses each year (Centers for Disease Control and Prevention, 2008b).

The prevalence of smoking, which is estimated at 1 billion worldwide, is slowly decreasing in industrialized countries and rising in developing countries, especially in Asia and Africa (Steptoe, et al., 2002). The worldwide death toll from smoking is expected to rise from 5 million to 10 million people per year by the year 2030 (Ezzati & Lopez, 2003). Data from the 2008 National Health Interview Survey (NHIS) reported that an estimated 20.6% of adults (46 million) in the United States are current cigarette smokers (Centers for Disease Control and Prevention, 2008a). Among these individuals,

smoking prevalence is slightly higher among men (23.1%) than women (18.3%). Although the prevalence is lower than reported in previous years, the rate of decline is not nearly sufficient to meet the National Health Service's objective to reduce the prevalence of cigarette smoking among adults to <12% (Centers for Disease Control and Prevention, 2006).

1.2 Erectile dysfunction

1.2.1 Prevalence and public health

Erectile dysfunction (ED) is defined in the DSM-IV-TR (American Psychiatric Association, 2000) as the recurrent inability to achieve or maintain adequate erection of the penis to engage in satisfactory sexual intercourse. Erectile dysfunction is estimated to affect 34 million men in the United States and more than 150 million men worldwide (Ayta, McKinlay, & Krane, 1999; Young, Bennett, Gilhooly, Wessells, & Ramos, 2002). By 2025 this prevalence is expected to double (Ayta, et al., 1999). Erectile dysfunction is considered a significant public health problem and has a strong negative effect on interpersonal relationships (Morokoff & Gillilland, 1993), well-being (Laumann, Paik, & Rosen, 1999), and quality of life (Fugl-Meyer, Lodnert, Branholm, & Fugl-Meyer, 1997; MacDonaugh, Ewings, & Porter, 2002).

Prevalence, incidence, and severity of ED all increase with age. In a national probability sample of 1,410 men in the United States, Laumann, Paik, and Rosen (1999) reported that approximately 7% aged 18-29 years, 9% aged 30-39 years, 11% aged 40-49 years, and 18% aged 50-59 years have erectile difficulties. A more recent cross-sectional analysis of 2,126 men in the Unites States (Selvin, Burnett, & Platz, 2007) revealed a

similar age-associated ED prevalence: approximately 5% aged 20-39 years, 15% aged 40-59 years, 44% aged 60-69 years, and 70% over 70 years had erectile difficulties. Of the relatively limited studies that have evaluated the prevalence of ED in countries other than the United States, all have reported similar age-associated rates (Martin-Morales, et al., 2001; Ponholzer, et al., 2005; Shirai, et al., 1987; Solstad & Hertoft, 1993)

1.2.2 Associated risk factors

Erectile dysfunction can be classified as either organic or psychogenic (Benet & Melman, 1995). Organic ED may be caused by vascular or neurological diseases, hormonal irregularities, or by abnormalities or lesions of the penile smooth musculature (Melman & Gingell, 1999). Psychogenic ED is inhibition of the erectile mechanisms via central mediation and has no physical underpinnings (i.e., purely cognitive cause). It is recognized that in most patients with ED, both organic and psychogenic components exist (Melman & Gingell, 1999).

It is now recognized that vascular diseases of the penile arteries are the most common causes of organic ED and account for up to 80% of cases (Donatucci & Lue, 1993; D. R. Kaiser, et al., 2004; O'Kane & Jackson, 2001). Atherosclerotic disease is the cause of approximately 40% of men older than 50 years with ED (F. E. Kaiser, et al., 1988). In patients with diabetes mellitus, the prevalence of ED ranges from approximately 40 - 50% (Chew, Earle, Stuckey, Jamroziki, & Keogh, 2000; McCulloch, Campbell, Wu, Prescott, & Clarke, 1980). This is irrespective of type of diabetes, but is dependent on patient age, duration of disease, and disease severity (Melman & Gingell, 1999). Other medical conditions associated with a high prevalence of ED include

multiple sclerosis (Ghezzi, Malvestiti, Baldini, Zaffaroni, & Zibetti, 1995), Alzheimer's disease (Zeiss, Davies, Wood, & Tinklenberg, 1990), renal failure (Kaufman, Hatzichristou, Mulhall, Fitch, & Goldstein, 1994), hepatic failure (Bortolotti, Parazzini, Colli, & Landoni, 1997), hyperlipidemia (Ponholzer, et al., 2005), and chronic obstructive lung disease (Fletcher & Martin, 1982; Köseoğlu, et al., 2005). Endocrine disorders, such as hypothyroidism and hypogonadism, may also induce ED (Soran & Wu, 2005), as may prostate disease and prostate surgery (Melman & Gingell, 1999).

Many medications and recreational drugs are associated with organic ED. However, it is often difficult to delineate whether the pharmacological agent, or the condition for which the drug is being taken, is primarily responsible. Benzodiazepines and certain diuretics unequivocally contribute to ED (Derby, Babour, Hume, & McKinlay, 2001). Selective serotonin reuptake inhibitors (SSRIs) (Lane, 1997; R. C. Rosen, Lane, & Menza, 1999) have also been demonstrated to induce ED.

Among lifestyle factors, smoking (Tengs & Osgood, 2001), obesity (Derby, et al., 2000), and physical inactivity (Derby, et al., 2000) have been associated with elevated risk for ED. Mixed results have been reported on the relation between alcohol consumption and male sexual dysfunction (Cornely, Schade, Van Thiel, & Gavaler, 1984; Jensen, 1984; Schiavi, Stimmel, Mandelli, & White, 1995; Whalley, 1978).

Psychogenic erectile dysfunction is much more prevalent in younger men and accounts for up to 70% of patients younger than 35 years and only 10% of men older than 50 years (Slag, et al., 1983). Some risk factors affecting psychogenic ED include performance anxiety, stress, depression, relationship difficulties, and anger suppression

(Araujo, Durante, Feldman, Goldstein, & McKinlay, 1998; Feldman, Goldstein, Hatzichristou, Krane, & McKinlay, 1994; Lue, 2000; Melman & Gingell, 1999; R. C. Rosen, 2001).

1.3 The link between cigarette smoking and erectile dysfunction

1.3.1 Extant smoking

Epidemiological studies demonstrate a clear link between cigarette smoking and sexual dysfunction in men. Large cross-sectional studies (Dorey, 2001; He, et al., 2007; Jeremy & Mikhailidis, 1998; Lam, Abdullah, Ho, Yip, & Fan, 2006; Mannino, Klevens, & Flanders, 1994; Ponholzer, et al., 2005) indicate that chronic smokers are approximately 1.5 to 2 times as likely as nonsmokers to report ED, even after controlling for age and confounding cardiovascular risk factors. In fact, a meta-analysis of 19 studies ($N = 3819$) over two decades revealed that 40% of men with ED were current smokers compared with 28% of men in the general population (Tengs & Osgood, 2001). Interestingly, it has been reported that the magnitude of association between smoking and ED decreases across increasingly older age groups. This suggests that smoking may have a stronger deleterious effect on sexual functioning in young male smokers compared to older male smokers (Gades, et al., 2005).

To my knowledge, only one study has longitudinally investigated the association between smoking and ED (Feldman, et al., 2000). Over 500 men reporting no lifetime incidence of diabetes, heart disease or cardiovascular conditions, and with no erectile dysfunction, were assessed at baseline. A follow up 8 years later indicated that smokers

were approximately 2 times as likely than nonsmokers to have moderate or complete erectile dysfunction (24% versus 14%; adjusted odds ratio = 1.97).

1.3.2 Prior smoking

Several cross-sectional studies have demonstrated an association with prior smoking and current ED (Bortolotti, et al., 1997; Mannino, et al., 1994; Mirone, et al., 2002). In an extensive review of the literature concerning ED and chronic tobacco use (McVary, Carrier, Wessells, & Subcommittee on Smoking and Erectile Dysfunction Socioeconomic Committee Sexual Medicine Society of North America, 2001), it has been shown that the nearly two-fold risk of ED decreases substantially in the initial 2-3 years after successfully quitting. Thereafter, the risk reduction decelerates, taking a full 10 years post-cigarette cessation for former smokers to achieve the risk level of never-smokers. However, a prospective study found no change in ED status among individuals who quit smoking for 8 years (Derby, et al., 2000), suggesting permanent smoking-induced vascular damage.

1.3.3 Passive smoking

Evidence also suggests an association between passive smoking and erectile function, with men exposed to passive smoke exposure having twice the risk of developing ED (Feldman, et al., 2000). Passive smoking may also reduce coronary flow velocity in healthy nonsmokers, potentially leading to endothelial dysfunction (Otsuka, et al., 2001). Regular passive exposure to tobacco smoke at home or work also increases the risk of coronary heart disease among nonsmokers (Kawachi, et al., 1997). Therefore, it is

reasonable to believe that passive smoking may induce erectile difficulties by precipitating vascular diseases.

1.3.4 Dose response

The dose-dependent relationship between cigarette smoking and ED has been explored in several studies and results appear to demonstrate an association between the intensity of cigarette smoking and severity of erectile difficulties. Specifically, heavy smokers appear to exhibit a higher risk of ED compared to moderate or light smokers (Gades, et al., 2005; Mirone, et al., 2002; Natali, Mondaini, Lombardi, Del Popolo, & Rizzo, 2005). In one particular study, Natali and colleagues (2005) demonstrated that the prevalence of ED is 2.5 times higher in heavy smokers compared to light smokers (43% vs. 17%, respectively). Conversely, other studies have found no differential risk of ED associated with the number of years smoked or the number of cigarettes smoked daily (Feldman, et al., 1994; Mannino, et al., 1994).

1.4 Penile erection physiology

1.4.1 Hemodynamics

Genital vasocongestion in the human male is a complex neurovascular event and has been reviewed extensively (Andersson & Wagner, 1997). Penile erection and detumescence are characterized by complementary hemodynamic processes (Taub, Lerner, Melman, & Christ, 1993). In the flaccid state, the cavernous smooth musculature and the smooth muscles of the arteriolar walls are tonically contracted, thereby enabling only a small amount of arterial inflow necessary for oxygenation (Dean & Lue, 2005).

After sexual stimulation (cognitive or somatic), the parasympathetic nervous system triggers the release of neurotransmitters from cavernous nerve terminals. This results in a decrease in peripheral resistance due to vasodilation and increased arterial inflow. Simultaneously, compression of the subtunical venular plexuses reduces venous outflow, resulting in penile engorgement and erection (Dean & Lue, 2005). Penile detumescence is largely under sympathetic nervous system control, which returns arterial blood flow to its prestimulation level, opens venous outflow channels, decreases intracavernosal pressure, and deactivates the veno-occlusive mechanism, returning the penis to its flaccid state (Melman & Gingell, 1999).

1.4.2 Neurotransmission and neuropeptide factors

In response to sexual stimulation, the parasympathetic nervous system triggers the release of acetylcholine which binds to cholinergic receptors on the corpus cavernosum (Meston & Frohlich, 2000), causing smooth muscle relaxation. Additionally, the cavernous nerves and endothelial cells release nitric oxide (NO) which has been identified as the principal neurotransmitter mediating penile erection (Burnett, Lowenstein, Bredt, Chang, & Snyder, 1992; Kim, Azadzoi, Goldstein, & Saenz de Tejada, 1991). Endothelial cells within the penis produce NO with enzyme nitric oxide synthase (eNOS). Enzyme nitric oxide synthase isoforms convert L-arginine to NO and other biochemical constituents (McVary, et al., 2001). Nitric oxide promotes the production of cyclic guanosine monophosphate (cGMP) in the vascular system (R. C. Rosen & McKenna, 2002). The interplay between NO and cGMP is responsible for relaxing cavernous smooth muscle cells and increases arterial inflow to the sinusoids,

promoting penile tumescence while also decreasing venous outflow. Detumescence, on the other hand, is modulated by the sympathetic nervous system via the release of norepinephrine and activation of postsynaptic α1-adrenergic receptors (Lincoln & Cornell, 1991).

Several neuropeptides interact with the NO dependent pathways of erectile function. Corporal endothelial cells synthesize and release endothelin, which acts as a vasoconstrictor and precipitates the contractile responses of the penile musculature (Saenz de Tejada, Carson, de las Morensas, Goldstein, & Traish, 1991). Vasoactive intestinal polypeptide has also been implicated in the biochemical pathways of erectile function (Melman & Gingell, 1999).

1.4.3 Endocrine factors

Testosterone plays a major role in men's sexual function and influences the growth and development of the male reproductive tract and secondary sex characteristics. The effects of androgens on libido and sexual behavior are well established. Testosterone regulates sexual desire, frequency of sexual activity, frequency of nocturnal erections, and erectile responses (Traish, Kim, Traish, & Kim, 2005). Decreased testosterone has been associated with erectile impairments (Guay, 2006). Studies in castrated animals have reported a decreased arterial inflow, venous leakage, and dramatically reduced erectile response (Mills, Stopper, & Wiedmeier, 1994; Penson, Ng, Cai, Rajfer, & Gonzalez-Cadavid, 1996). Importantly, studies have also demonstrated that the addition of testosterone, and its conversion to dihydrotestosterone, can restore erectile function (Baba, Yajima, Carrier, Akkus, et al., 2000; Baba, Yajima, Carrier, Morgan, et al., 2000).

It appears that testosterone achieves this by peripheral mechanisms (endothelial dependent and independent) and central mechanisms. Testosterone replacement therapy is therefore effective for erectile dysfunction in men with hypogonadism, with success rates of 35-40% (Guay, 2006).

1.4.4 Central nervous system

Studies in both animals and humans have helped to elucidate several brain areas that play a role in erection physiology. Studies in animals have delineated the important function of the medial preoptic area (MPOA) and the paraventricular nucleus (PVN) of the hypothalamus and hippocampus. In fact, electrostimulation of this area induces penile tumescence, and lesions at this site limit copulation (Marson, Platt, & McKenna, 1993). Several brainstem and medullary regions, as well as the forebrain are also involved in sexual function (Meston & Frohlich, 2000).

1.5 Effects of tobacco smoke/nicotine on mechanisms underlying male sexual arousal

Pathophysiological underpinnings of tobacco-induced ED have been proposed in response to the wide range of research examining the effects of cigarette smoking on biochemical mechanisms underlying vascular functioning (Mazo, Gamidov, Anranovich, & Iremashvili, 2005). Nicotine (which is the most important compound responsible for acute cardiovascular effects of smoking) increases heart rate, myocardial contractability, and blood pressure - effects which are primarily due to stimulation of sympathetic neurotransmission. Cigarette smoking decreases penile arterial inflow (McMahon &

Touma, 1999) and disrupts veno-occlusive mechanisms (Elhanbly, et al., 2004), resulting in deficiency of genital vasoengorgement. These disruptions are mediated by a deregulation in endothelium smooth muscle relaxation (Mazo, et al., 2005). Additionally, experimental evidence indicates that chronic nicotine exposure has deleterious effects on modulating the release of adrenaline and noradrenaline (Jeremy & Mikhailidis, 1998) which may compromise erectile functioning.

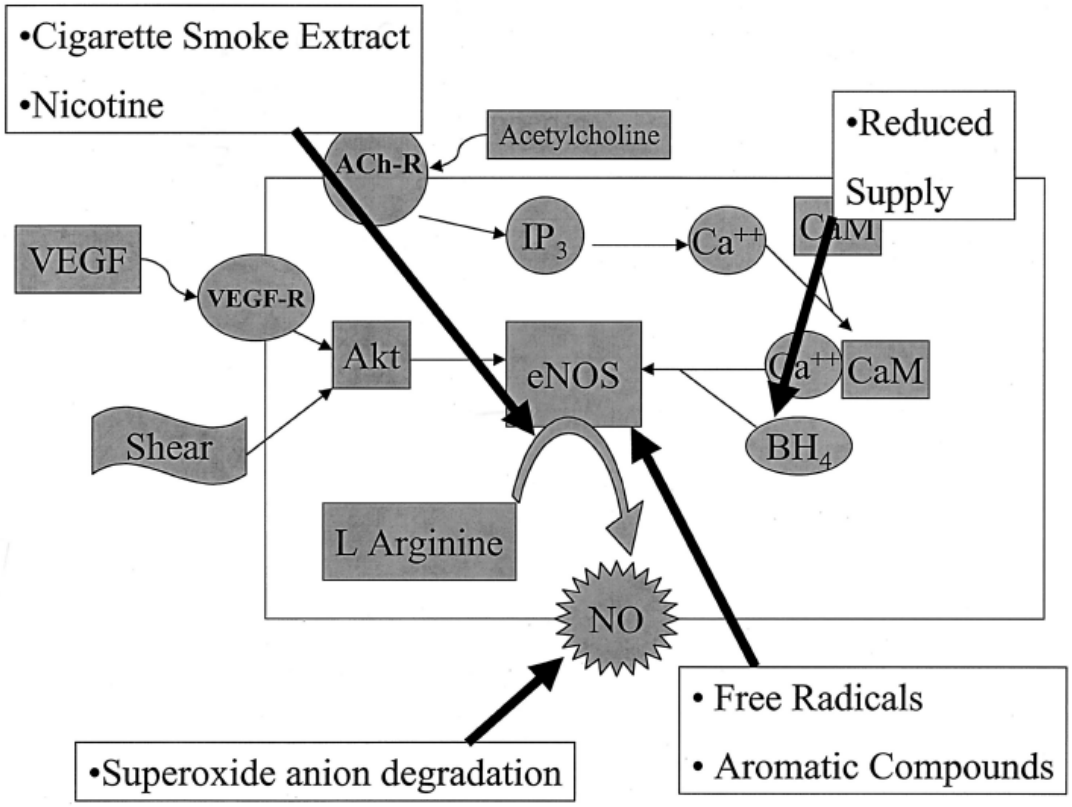

Figure 1. Presumed Mechanisms of Action Responsible for Smoking-Induced Altered Smooth Muscle Relaxation.

Free radicals and aromatic compounds diminish endothelial synthesis of nitric oxide (*NO*) by affecting enzyme nitric oxide synthase (*eNOS*), causing impaired endothelium dependent relaxation of arteries. This may result from reduction in activity of endothelial nitric oxide synthase that is attributable to inadequate supply of coenzyme tetrahydrobiopterin. Smoke also causes contraction of smooth muscle by superoxide anion mediated degradation of nitric oxide. *Ach-R*, acetylcholine receptor. *VEGF*, vascular endothelial growth factor. *VEGF-R*, vascular endothelial growth factor receptor. *IP3*, 1,4,5-triphosphate. Figure and Figure caption from McVary and colleagues (2001).

Biochemical processes underlying erection physiology may also be affected by chronic smoking. Nitric oxide produced within penile endothelial cells has been identified as the principal neurotransmitter mediating erection (Burnett, et al., 1992; Kim, et al., 1991). Free radicals and other compounds within cigarettes may decrease the endothelial synthesis of NO directly, or indirectly by targeting precursors (disrupting the activity of enzyme nitric oxide synthase (eNOS) thereby disrupting the conversion of L-arginine to NO), resulting in decreased penile blood inflow (see Figure 1) (McVary, et al., 2001; Zhang, Venardos, Chin-Dusting, & Kaye, 2006). This may have significant long-term effects on erectile functioning. Tobacco inhalation also exerts neuroendocrine effects, affecting pituitary, thyroid, adrenal, and testicular function (Kapoor & Jones, 2005), which may affect erectile responses.

In sum, nicotine and/or particular tobacco compounds may deleteriously affect the mechanisms underlying sexual arousal in the following ways: (i) centrally, by eliciting dose-dependent neurotransmitter and neuroendocrine effects (Pomerleau, 1992); (ii) peripherally, by acting as a sympathetic nervous system (SNS) agonist (Haass & Kübler, 1997); or (iii) by disrupting NO synthesis directly or indirectly by targeting biochemical precursors. Complex interactions among these pathways may also exist (Sartori, Lepori, & Scherrer, 2005).

1.6 Acute effects of tobacco smoke on male sexual arousal

Few studies have focused on the acute effects of smoking on physiological sexual response. One animal study (Juenemann, et al., 1987) assessed the effects of 7 to 12 minutes of acute smoke exposure on penile erection in dogs. After smoke ingestion

equivalent to 2 to 3 cigarettes, 5 of 6 dogs did not achieve complete erection during neurostimulation. Both arterial inflow via the internal pudental artery and veno-occlusion ability were impaired, with almost complete ineffectiveness of venous restriction. Additionally, the same phenomena were observed after intravenous administration of pure nicotine. Another study investigated the effect of 8 weeks of passive smoking on erectile functioning in rats. Although eNOS expression was reduced, no impairment of erection was demonstrated during neurostimulation (Xie, Garban, Ng, Rajfer, & Gonzalez-Cadavid, 1997).

To my knowledge, there has only been one experimental study involving the acute effects of cigarette smoking on human sexual arousal. Gilbert, Hagen and D'Agostino (1986) tested 42 male smokers who were randomly assigned to nicotine, placebo, or wait list conditions. Participants who smoked three 0.9-mg nicotine cigarettes within one half-hour – relative to men who smoked three placebo cigarettes, and to men who had not smoked – experienced significantly attenuated physiological sexual arousal.

1.7 Acute effects of nicotine on male sexual arousal

Experimental studies examining acute effects of tobacco inhalation on physiological sexual arousal help to elucidate underlying physiological mechanisms that may be responsible for introducing and/or maintaining erectile impairment. However, because chronic cigarette smoking may cause vascular duration-dependent degeneration (Pittilo & Woolf, 1993), uncertainty arises as to whether the acute effects of tobacco smoke on sexual arousal differentially affect long-term smokers compared to nonsmokers. Additionally, because cigarettes contain over 4000 active pharmacological

constituents (Chien, 1994), the primary element or group of interacting compounds responsible for the deleterious effects of smoking on sexual response remains unclear.

In an attempt to address these issues, Harte and Meston (2008a) conducted the first empirical investigation examining the acute effects of isolated nicotine on sexual arousal in nonsmoking men measured both physiologically and subjectively. Twenty-eight sexually functional heterosexual men, each with less than 100 direct exposures to nicotine, participated in a double-blind, randomized, placebo-controlled, crossover trial. Participants received either 6mg of nicotine gum (approximately equivalent to smoking one high-yield cigarette) or placebo gum approximately 40 minutes prior to viewing an erotic film. Results indicated that nicotine, compared to placebo, significantly reduced erectile responses to the erotic films, corresponding to a 23% reduction in physiological sexual arousal. Nicotine had no significant effect on subjective ratings of sexual arousal, or on mood.

These findings suggest that the reduction in physiological sexual response resulting from nicotine intake was not likely mediated by nicotine-induced changes in cognitive states. This further supports the hypothesis that nicotine may directly or indirectly precipitate genital hemodynamic disruption via peripheral or central activation of the nervous system. This finding was in accordance with those of other studies examining the deleterious acute effects of isolated nicotine on sexual arousal (Klinge, Alaranta, & Sjöstrand, 1988) and peripheral vasculature (Chalon, Moreno, Benowitz, Hoffman, & Blaschke, 2000). Although this study indicated that nicotine impairs sexual

arousal acutely in healthy, sexually functional, nonsmokers, it is unknown whether these results generalize to individuals who are long-term smokers.

1.8 Effects of smoking cessation on erectile function

1.8.1 Prior studies

Considering the robust evidence demonstrating the link between cigarette smoking and ED, an intervention that has the broadest health impact is smoking cessation. To my knowledge only two studies have investigated the effects of smoking cessation on erectile function. Sighinolfi and associates (2007) tested 20 heavy smokers (20 to 40 cigarettes/day), who had all been smoking for at least five years, and who met criteria for ED according to an established questionnaire. Penile hemodynamic responses were measured with Doppler ultrasonography during baseline (while smoking) and acute follow-up (while smoke-free). Results indicated a significant improvement in penile blood flow within 24 to 36 hours of smoking discontinuation, suggesting that quitting smoking can potentially facilitate the remission of ED.

Similarly, Guay and colleagues (1998) measured nocturnal penile tumescence and rigidity in 10 male smokers via a portable home monitor. Results showed significant improvement 24 hours after smoking cessation for both penile rigidity and tumescence. Of the 10 patients, 100% displayed improvements in both base and tip tumescence; 90% and 100% exhibited improvements in base and tip rigidity, respectively. They also assessed four men 1 month later, a period during which they wore a daily 21-mg nicotine transdermal patch. Examination of mean responses indicated a trend for continued improvement. Examining the four cases individually, it was shown that 2 of 4 men

displayed the highest tumescence during the nicotine patch regimen, the lowest tumescence during smoking, and a moderate level of tumescence during smoking cessation. The other two men displayed similar levels of tumescence during the patch treatment and while smoking, with enhanced tumescence during smoking cessation. With respect to rigidity, 3 of 4 men demonstrated a pattern characterized by lowest rigidity during smoking, moderate rigidity during nicotine treatment, and highest rigidity while not smoking. Guay and colleagues (1998) concluded that smoking-induced ED may not necessarily be due to the presence of nicotine, but rather caused by other psycho-pharmacologically active ingredients found within cigarettes (e.g., carbon monoxide, tar, noxious gases). It should be noted that involuntary erection (nocturnal penile tumescence) was measured, and therefore how isolated nicotine and cigarette smoking affects voluntary sexual arousal (in response to erotic stimulation) remains unknown.

1.8.2 Limitations

These studies provide an excellent foundation for examining the relationship between smoking and sexual health; however, they are not without their limitations. First, these studies have only assessed individuals with clinically diagnosed erectile dysfunction, and therefore it remains unclear how smoking cessation affects sexual arousal responses in nonclinical individuals. Considering that the majority of smokers (under 60 years of age) would be expected to *not* have ED, it is important to investigate the association between smoking cessation and sexual health among all men, both with and without erectile difficulties.

Second, these studies have only included one outcome measure (physiological sexual arousal). Although improvement in erectile capacity was demonstrated in these studies, it is unclear how these physiological changes correspond to changes of a clinical nature. That is, does a *statistically* significant improvement in penile response translate to a *clinically* significant change, such that a patient either does not meet criteria for ED, or at least significantly improves his sexual health as assessed by validated construct-specific measures? Incorporating gold-standard self-report measures of sexual arousal and sexual functioning would help address these questions and would be an ecologically valid way of assessing changes in sexual health.

Third, these studies have only tested acute effects (24 – 36 hours) of quitting smoking and have not tested men at a later follow-up. Moreover, because of the acute nature of these follow-up assessments, these studies tested men who quit smoking spontaneously ("cold-turkey"). Therefore, it is reasonable to believe that both physiological and psychological nicotine withdrawal effects could have affected results. With this in mind, it may be important for studies to assess sexual functioning in men at a later follow-up period, after they have *successfully* quit smoking and are no longer experiencing undesirable side effects.

Fourth, these studies have only included a treatment group comprised of individuals undergoing the cessation process; that is, these studies have not compared an experimental group to a control condition. As such, it remains uncertain as to whether changes in erectile response are primarily attributable to smoking cessation, or rather to potential confounding variables (e.g., threats to internal validity such as testing effects).

Fifth, because long-term cigarette smoking can cause vascular degeneration (Pittilo & Woolf, 1993; Powell, 1998), it is reasonable to believe that smoking cessation may differentially enhance smokers' sexual arousal responses as a function of their lifetime cigarette consumption. Future studies would benefit from statistically controlling for the number of pack years for which a participant has smoked. It is the goal of this study to redress these limitations.

CHAPTER 2: THE PRESENT STUDY

2.1 Brief overview

The present study attempted to examine the effects of smoking cessation on sexual health in long-term smoking men. Physiological and self-reported indices of sexual health, as well as autonomic activity were assessed at three time intervals: (i) at baseline, while participants were regularly smoking; (ii) at mid-treatment, while using a 21-mg nicotine transdermal patch; and (iii) at follow-up, four weeks after nicotine patch cessation. To my knowledge, this is the first study examining sexual function and smoking cessation that: (i) recruited individuals with and without erectile dysfunction; (ii) used several indices of sexual health measured psychophysiologically (erectile tumescence, continuous subjective arousal), and by self-report (erectile function, sexual satisfaction, sexual desire); (iii) assessed for clinical significance with respect to self-report measures of sexual function; (iv) assessed intermediate (i.e., 4 weeks post-cessation) effects of smoking cessation with respect to indices of sexual health; and (v) compared outcome measures between successful quitters and those who relapsed.

2.2 Specific aims and hypotheses

Aim 1: To investigate within- and between-group changes in physiological sexual arousal. Among successful quitters, it was hypothesized that these participants would display significantly higher physiological arousal responses during post-cessation follow-up, compared to both the mid-treatment assessment (while using a 21-mg nicotine patch) and the pre-treatment assessment (while smoking regularly). Furthermore, it was believed

that these participants would show increased physiological sexual arousal at mid-treatment compared to pre-treatment (as a function of eliminating habitual intake of noxious gases found in cigarette smoke). I was uncertain as to whether this difference would be statistically significant, as nicotine alone may play an important role in inhibiting sexual arousal (Harte & Meston, 2008a, 2008c).

With respect to the entire sample of participants (both successful and unsuccessful quitters), I expected that there would be no between-group differences at baseline and mid-treatment. However, it was expected that at follow-up, successful quitters would display significant increases in physiological sexual arousal responses compared to relapsers.

Aim 2: To investigate within- and between-group changes in continuous subjective sexual arousal. To my knowledge, no studies have investigated the effects of smoking cessation on self-reported sexual arousal. In nonsmoking men without ED, it has been shown that continuous measurements of subjective sexual arousal remained unaffected despite reduction in genital arousal (Harte & Meston, 2008a). This may suggest that nicotine attenuates genital arousal directly via physiological mechanisms, rather than impacting cognitive processes. However, it is unknown how smoking may affect self-reported arousal in habitual smokers or men with erectile difficulties. It is possible that over time, smokers may synchronize their self-reported sexual arousal to match their inhibited physiological sexual arousal. In other words, because men have a relatively salient physiological feedback system (i.e., penile erection), visuosensory

awareness of genital arousal provides significant feedback for subjective appraisals of sexual arousal (Sakheim, Barlow, Beck, & Abrahamson, 1984).

It was hypothesized that all participants would demonstrate the same within- and between-group patterns of both subjective sexual arousal and physiological sexual arousal. Thus, among successful quitters, subjective sexual arousal was expected to increase as a result of smoking cessation, resulting in no between-group differences at baseline and mid-treatment, but significant group differences at follow-up.

Aim 3: To investigate within- and between-group changes in self-reported sexual function. It was also hypothesized that erectile functioning measured via a self-report questionnaire (the International Index of Erectile Function (IIEF); (R. C. Rosen, et al., 1997)) (see Appendix A) would show a similar pattern of within- and between-group results as compared to sexual arousal measured physiologically. Specifically, it was hypothesized that successful quitters would display significantly higher mean self-reported erectile functioning scores at follow-up compared to both the pre-treatment and mid-treatment assessments. Additionally, I expected that the proportion of successful quitters meeting criteria for erectile dysfunction (as per the IIEF) would significantly decrease from baseline to both mid-treatment and follow-up.

Among successful quitters, orgasmic function, intercourse satisfaction, and overall sexual function domains of the IIEF were also expected to increase in a statistically significant pattern similar to the erectile functioning domain. Finally, sexual desire and overall satisfaction domains were expected to show similar across session

patterns; however I was uncertain as to whether any of these changes would be statistically significant.

With respect to unsuccessful quitters, it was expected that these individuals would show no across-session changes on any of the IIEF domains, resulting in group×time interaction effects for each sexual function variable. An overview of all general aims and specific hypotheses regarding specific outcome variables associated with each general aim are shown in Tables 1 and 2.

2.3 Potential implications

If successful quitters (compared to unsuccessful quitters) do in fact demonstrate a significant increase in sexual function as a result of smoking cessation, the results of this project may serve as a novel means to facilitate programs and interventions targeting the prevention and cessation of cigarette smoking in men. In particular, it is my hope that the results herein may influence healthcare providers to discuss the benefits of quitting smoking with male patients. Enhancing successful smoking cessation in men would significantly enhance quality of life, substantially reduce premature death, and alleviate enormous economic burdens caused by smoking-related diseases.

Outcome measures	Comparison		
	Mid-treatment vs. **baseline**	**Follow-up** vs. **baseline**	**Follow-up** vs. **mid-treatment**
Aim 1 – Indices of physiological sexual arousal			
Magnitude of change in penile tumescence (cm)	?	↑	↑
Percent change in penile tumescence	?	↑	↑
Maximum arousal (cm)	?	↑	↑
Percent change in maximum arousal	?	↑	↑
Latency to reach maximum arousal (sec)	?	↓	↓
Rate of onset to maximum erection (slope)	?	↑	↑
Aim 2 – Indices of self-reported sexual arousal			
Percent change in arousal	?	↑	↑
Latency to reach maximum arousal (sec)	?	↓	↓
Rate of onset to maximum arousal (slope)	?	↑	↑
Aim 3 – Indices of self-reported sexual functioning*			
Mean erectile function score	?	↑	↑
Mean orgasmic function score	?	↑	↑
Mean sexual desire score	?	?	?
Mean intercourse satisfaction score	?	↑	↑
Mean overall satisfaction score	?	?	?
Mean overall sexual functioning (total score)	?	↑	↑
Percentage meeting criteria for ED†	?	↓	↓

Table 1. Overview of Aims and Hypotheses for the Subgroup of Successful Quitters.

Upward arrows indicate statistically significant increases. Downward arrows indicate statistically significant decreases. Question marks denote uncertainty regarding statistical significance. All hypotheses pertain to the group of successful quitters Unsuccessful quitters were not expected to show any across-session changes.

Abbreviations: ED = erectile dysfunction

*As per the International Index of Erectile Function (IIEF).

†According to an IIEF-erectile function cutoff score of 25.

Outcome measures	Time point		
	Baseline	Mid-treatment	Follow-up
Aim 1 – Indices of physiological sexual arousal			
Magnitude of change in penile tumescence (cm)	SQ = UQ	SQ = UQ	SQ > UQ
Percent change in penile tumescence	SQ = UQ	SQ = UQ	SQ > UQ
Maximum arousal (cm)	SQ = UQ	SQ = UQ	SQ > UQ
Percent change in maximum arousal	SQ = UQ	SQ = UQ	SQ > UQ
Latency to reach maximum arousal (sec)	SQ = UQ	SQ = UQ	SQ < UQ
Rate of onset to maximum erection (slope)	SQ = UQ	SQ = UQ	SQ > UQ
Aim 2 – Indices of self-reported sexual arousal			
Percent change in arousal	SQ = UQ	SQ = UQ	SQ > UQ
Latency to reach maximum arousal (sec)	SQ = UQ	SQ = UQ	SQ < UQ
Rate of onset to maximum arousal (slope)	SQ = UQ	SQ = UQ	SQ > UQ
Aim 3 – Indices of self-reported sexual functioning*			
Mean erectile function score	SQ = UQ	SQ = UQ	SQ > UQ
Mean orgasmic function score	SQ = UQ	SQ = UQ	SQ > UQ
Mean sexual desire score	SQ = UQ	?	?
Mean intercourse satisfaction score	SQ = UQ	SQ = UQ	SQ > UQ
Mean overall satisfaction score	SQ = UQ	?	?
Mean overall sexual functioning (total score)	SQ = UQ	SQ = UQ	SQ > UQ
Percentage meeting criteria for ED†	SQ = UQ	SQ = UQ	SQ < UQ

Table 2. Overview of Aims and Hypotheses for Between-Group Analyses of all Participants.

Question marks denote uncertainty regarding statistical significance.

Abbreviations: ED = erectile dysfunction; SQ = successful quitters; UQ = unsuccessful quitters.

*As per the International Index of Erectile Function (IIEF).

†According to an IIEF-erectile function cutoff score of 25.

CHAPTER 3: RESEARCH DESIGN, MATERIALS, AND METHODS

3.1 Overview of experimental design

This was a 12-week treatment study examining the effects of a smoking cessation intervention on sexual arousal responses in men. After participating in an initial telephone screening, participants who expressed a committed desire to quit smoking were invited to the Sexual Psychophysiology Laboratory at the University of Texas at Austin, and multimodal assessments of sexual functioning were conducted. Participants were re-assessed at mid-treatment, while using a nicotine patch, and at 1-month follow-up.

3.2 Participants

3.2.1 Overview of participants

Long-term male smokers ($N = 65$) aged 23-60, irrespective of erectile functioning, and who were motivated to quit smoking, were recruited through online advertisements, and via flyers throughout the Austin, Texas area. During the telephone screening, smoking participants were questioned on their pre-smoking sexual functioning and only those individuals who reported no sexual dysfunction prior to smoking onset were eligible to enroll in the study. Subject inclusion and exclusion criteria are listed below along with a brief description of the rationale underlying several key decisions concerning subject selection. All medical exclusionary criteria were based on self-report rather than via medical records.

3.2.2 Inclusion/exclusion criteria

Inclusion criteria for participants were as follows:

1) *Men aged 23-60 years.* The lower age limit of 23 years was implemented in order to allow sufficient time for participants to smoke legally for at least 5 years (see criterion 5). The upper age criterion is implemented in order to minimize the age-associated increase in the prevalence of erectile impairment, irrespective of smoking (see Laumann et al. (1999), and Selvin et al. (2007) for review).
2) *Proficient in English.* Participants were required to be fluent in English in order to enroll in the study because most of the self-report instruments have not been translated or validated in languages other than English, and there are no appropriate alternative instruments that meet this criterion.
3) *Heterosexual.* Only heterosexual participants were recruited because the gold-standard sexual function measure has not been validated within gay or bisexual populations. Heterosexuality will be operationally defined as self-report of exclusive, or predominant opposite gender sexual feelings and/or behaviors (i.e., scores of 0, 1, or 2) as assessed using the Kinsey Sexual Orientation Scale (see Appendix B) (Kinsey, Pomeroy, & Martin, 1948).
4) *Involved in a heterosexual relationship in which a participant is willing to engage in at least one sexual encounter per week.* This was to ensure sufficient opportunity to assess the clinical benefits of smoking cessation in the patients' natural setting. Furthermore, the erectile function measure

(International Index of Erectile Function (IIEF) (R. C. Rosen, et al., 1997)) required that participants be sexually active with a partner.

5) *Smoking at least 15 cigarettes per day cigarettes for a minimum of 5 consecutive years.* This was to ensure that participants had sufficient exposure to tobacco smoke.
6) *No sexual dysfunction prior to smoking onset.*
7) *Motivated and committed to quit smoking.*

Exclusion criteria for participants were as follows:

1) *Under the age of 23 or over the age of 60.* see inclusion criteria above.
2) *History of HIV infection or active, untreated pelvic or urinary tract infection including, sexually transmitted diseases such as chlamydia genital herpes, gonorrhea, or syphilis.*
3) *Major pelvic surgery that may have caused nerve damage, or serious bladder, rectal, or abdominal surgery*. This was to rule out underlying neural conditions as a cause for erectile difficulties.
4) *Neurological impairment due to diabetes, stroke, pelvic nerve damage secondary to trauma, cancer treatments, myasthenia gravis, multiple sclerosis or spinal cord damage*.
5) *Clinically significant untreated renal or endocrine disease*.

6) *Uncontrolled hypotension or hypertension* manifested by systolic blood pressure >170 or <90 mm Hg or diastolic blood pressure >100 or <50 mm Hg.

7) *History of serious drug abuse or serious alcohol abuse during the past 12 months.* To rule out serious drug and alcohol abuse and/or dependence, participants must score < 16 points on the Alcohol Use Disorders Identification Test (AUDIT; see Appendix C) (J. Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) and < 6 on the Drug Abuse Screening Test (DAST-10; see Appendix D) (Skinner, 1982).

8) *Evidence of schizophrenia, delusional disorder, or psychotic disorders not classified elsewhere.* This was to minimize the possibility that symptoms associated with these disorders could mask the therapeutic benefits of smoking cessation on sexual function.

9) Not involved in a heterosexual relationship in which an individual was willing to engage in at least one sexual encounter per week. See inclusion criteria above.

10) *Participants who posed a current, serious suicidal or homicidal risk.*

11) *Participants using medications known to affect sexual or vascular functioning.* These medications included antidepressants, anti-hypertensives, and hormone supplements, as well as sildenafil, vardenafil, tadalafil, or any other substance designed to affect sexual performance.

12) *Participants using insulin*, *narcotic pain relievers (propoxyphene, pentazocine), oxazepam, or medications for respiratory diseases such as chronic obstructive pulmonary disease or asthma (xanthines (e.g., theophylline)), as these drugs are contraindicated by the nicotine patch.*

13) *Participants using non-nicotine smoking cessation medications at time of enrollment (buproprion, varenicline).*

14) *Participants who report experiencing clinically significant sexual difficulties, including hypoactive sexual desire disorder, sexual arousal disorder, premature ejaculation, or inhibited orgasm prior to the onset of smoking.*

15) *Recent myocardial infarction, serious heart arrhythmias, and those with serious or worsening angina.*

16) *Hypersensitivity or allergy to nicotine, and/or allergy to adhesive tape or bandages.*

17) *History of or current psoriasis, dermatitis (atopic or eczematous), active peptic ulcers, severe renal impairment, hyperthyroidism, vasospastic diseases, pheochromocytoma, or insulin-dependent diabetes mellitus.*

3.3 Measures

3.3.1 Primary outcome measures

Physiological sexual arousal

Penile tumescence is considered the most sensitive index of sexual arousal and the most reliable measure of physiological response (R. C. Rosen & Keefe, 1978). Male genital arousal was assessed via penile circumferential change using a mercury-in-rubber

strain gauge (Hokanson, Inc., Bellevue, WA, USA) positioned mid-shaft on the penis. The signal was sampled at a rate of 80 samples/second, low-pass filtered (to 0.5 Hz), digitized (40 Hz), and recorded using the software package AcqKnowledge III, Version 3.73 (BIOPAC Systems, Inc., Santa Barbara, CA, USA) and a Model MP100WS data acquisition unit (BIOPAC Systems, Inc., Santa Barbara CA, USA).

Several indices of physiological sexual arousal were calculated during each visit: (i) mean penile tumescence during each film segment, which was converted to magnitude of within-session change; (ii) within-session percent change in penile tumescence; (iii) maximum arousal (largest circumferential measurement during the erotic film); (iv) percent change in maximum arousal; (v) latency to reach maximum arousal; and (vi) rate of onset to maximum erection (slope).

Self-reported sexual arousal

Genital responses alone can provide only a partial understanding of the complex interplay of physiological, cognitive, and behavioral factors that are responsible for the processing of, and responding to, sexually-relevant cues (R Rosen & Beck, 1988; Wincze, Hoon, & Hoon, 1977). As such, continuous measures of self-reported sexual arousal responses were additionally collected. These responses were measured using a hand-controlled device (Rellini, McCall, Randall, & Meston, 2005) which consisted of a computer optical mouse mounted on a wooden track divided into seven equally spaced intervals, where 0 indicated neutral, and 1–7 reflected increasingly higher levels of feeling sexually aroused. A software program written in MatLab (The MathWorks, Inc, Natick, MA, USA) detected the position of the pointer with respect to the *y*-axis of the

computer's monitor, and the signal was low-pass filtered (to 0.5 Hz), and digitized (40 Hz). Several indices of subjective sexual arousal were calculated for each visit and included: (i) mean self-reported arousal during each film segment; (ii) latency to reach maximum arousal; and (iii) rate of onset to maximum arousal (slope). This device has been shown to reliably measure subjective sexual arousal in a number of studies conducted in men (Harte & Meston, 2008a, 2008c).

Sexual function

Sexual function was assessed with the International Index of Erectile Function (IIEF; see Appendix A) (R. C. Rosen, et al., 1997), which is the most widely used psychometric index of self-reported erectile function. Because this measure provides an ecologically valid index of sexual function in the natural environment (i.e., sexual intercourse with a partner during the past month versus sexual functioning via laboratory-measured physiological responses), the IIEF was considered the primary subjective sexual health index in this study.

The IIEF is a 15-item measure assessing five-factor analytically derived areas of male sexual functioning: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. The measure allows for the calculation of specific indexes for each dimension as well as measure of overall sexual functioning (score ranges: erectile function: 1–30; orgasmic function: 0–10; desire: 2–10; intercourse satisfaction: 0–15; overall satisfaction: 2–10; total: 5–75). The IIEF has demonstrated acceptable internal reliability (Cronbach's alpha values of .73 and higher), test-retest reliability (r = .64 to r = .84), and validity (R. C. Rosen, et al., 1997) and has been

standardized on a sample of healthy and sexually dysfunctional men (Cappelleri, Rosen, Smith, Mishra, & Osterloh, 1999). An erectile function (EF) cutoff score of less than or equal to 25 has been demonstrated to have sensitivity of 0.97 and specificity of 0.88 to detect individuals with and without erectile dysfunction (Cappelleri, et al., 1999). Substantial agreement has been shown between these predicted and "true" classes (weighted kappa 0.80) (Cappelleri, et al., 1999). The severity of ED is also classified into five categories: no ED (EF score 26 to 30), mild (EF score 22 to 25), mild to moderate (EF score 17 to 21), moderate (EF score 11 to 16), and severe (EF score 6 to 10).

3.3.2 Cardiovascular measures

Heart rate

Heart rates were assessed using an Omron HEM-712C (Omron Healthcare, Inc, Bannockburn, IL, USA) automatic inflation digital blood pressure and pulse monitor. Continuous heart rates during the film sequence presentations were measured using an electrocardiograph with an augmented 3-limb lead site paradigm (upper right chest, lower left chest, right ankle) which connected to the BIOPAC MP100WS data acquisition unit.

Blood pressure

Systolic and diastolic blood pressures (in mm Hg) were assessed using an Omron HEM-712C automatic inflation digital blood pressure and pulse monitor with the cuff placed on each participant's non-dominant upper arm.

3.3.3 Anthropometric measures

Height and weight

Standing height was measured (without shoes) to the nearest 0.25 inch with a vertical stadiometer (Health-o-Meter, Sunbeam Products, Inc., Boca Raton, FL, USA), and weight was assessed to the nearest 0.1 lbs with a portable digital scale (Salter, Oak Brook, IL, USA). Body mass index (BMI) was calculated by diving each participant's weight (converted to kilograms) by the square of his height (converted to meters).

3.3.4 Moderating variables

Nicotine dependence

The Fagerstrom Test for Nicotine Dependence (FTND; see Appendix E) (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) is a widely used 6-item instrument for quantifying physical nicotine dependence in smokers. The FTND has satisfactory internal consistency (Cronbach's a =.64) and high test-retest reliability *(r* = .88) (Heatherton, et al., 1991). Findings indicate that the FTND correlates with biological measures of nicotine dependence (expired-air carbon monoxide levels, plasma nicotine levels, plasma cotinine levels). The FTND total score has a range of 0 to 10 points, and can be classified into five categories: very low addiction (0 to 2 points), low addiction (3 to 4 points), medium addiction (5 points), high addiction (6 to 7 points), and very high addiction (8 to 10 points).

Affect

The Positive and Negative Affect Schedule (PANAS; see Appendix F) (D. Watson, Clark, & Tellegen, 1988) was administered to examine whether changes in affect in response to smoking cessation may mediate sexual arousal responses (e.g., increased tension and/or irritability may distract one from processing sexually relevant cues, resulting in decreased sexual arousal). The PANAS is a brief self-report inventory and consists of two 10-item mood scales which provide measures of both positive and negative affect. These two dimensions are dispositional, with high negative affect reflecting subjective distress and unpleasurable engagement with the environment, and high positive affect indicative of pleasurable engagement with the environment. Low scores within each scale represent the absence of these dimension-specific high-valence feelings. Thus, emotions such as enthusiasm and alertness are characteristic of high positive affect, while sadness is reflective of low positive affect (D Watson & Clark, 1984).

Participants rated the extent to which they were experiencing each particular emotion at that given moment on a 5-point Likert scale ranging from 1 ("very slightly or not at all") to 5 ("extremely"). Scores were summed within each factor. The PANAS has demonstrated high internal consistency (Cronbach's alphas ranging from .84 to .90), acceptable test-retest reliability (r = .68 - .71) and validity (D. Watson, et al., 1988). When used with short-term instructions (e.g., a participant rating how he feels *right now* or *today*), the PANAS is sensitive to fluctuations in mood (D. Watson, et al., 1988).

Smoking history

It is reasonable to believe that smoking cessation may differentially enhance smoker's sexual arousal as a function of their lifetime cigarette consumption. Therefore, age at smoking onset, as well as the duration and frequency of cigarette consumption were assessed. Additionally, these data were converted to pack years, which is a term used to describe the amount a person has smoked over time. One pack year is defined as 20 manufactured cigarettes (1 pack) smoked per day for one year. Irrespective of lifetime smoking history, a participant's smoking frequency (cigarettes/day) at time of enrollment was also assessed.

3.3.5 Protocol monitoring

Nicotine patch compliance

Considering that nicotine may exert acute effects on sexual arousal in men (Harte 2008), participants' compliance with nicotine patch use was monitored throughout the study. Specifically, participants were asked on a weekly basis to report via telephone: (i) the frequency of patch use (number of days/week); (ii) the dose of each patch used (21mg, 14mg, 7mg); and (iii) the timing of each patch adherence and removal.

Intra- and post-treatment tobacco/nicotine use

Participants were asked on a weekly basis to report via telephone: (i) the number of cigarettes smoked per day during the prior week; (ii) the number of instances of nicotine replacement therapy (NRT) use other than the patch (i.e., nicotine gum, nicotine nasal spray, nicotine lozenge, nicotine inhaler).

Assessment of treatment side effects

The Systematic Assessment for Treatment Emergent Events (SAFTEE; see Appendix G) (Levine & Schooler, 1986) is a rating scale designed to collect and assess information on patient side effects during a clinical intervention study or clinical trial. The SAFTEE was administered to participants at mid-treatment (while participants were using a 21-mg nicotine transdermal patch), and immediately after they completed their 8-week patch regimen.

3.3.6 Screening measures

Alcohol use

Alcohol use was assessed with the Alcohol Use Disorders Identification Test (AUDIT; see Appendix C) (J. Saunders, et al., 1993). The AUDIT is a brief 10-item screening scale that assesses three conceptual domains: alcohol consumption (3 items), alcohol dependence (3 items), and adverse consequences of alcohol use (4 items). The AUDIT has demonstrated acceptable internal consistency (Cronbach's alphas above .80) (Allen, Litten, Fertig, & Babor, 1997; Reinert & Allen, 2002), test-retest reliability (r = .64 - .92) (Reinert & Allen, 2002), and acceptable validity. It has also been shown to be appropriate for use with people from a variety of ethnic groups (Reinert & Allen, 2002). Scores on the AUDIT correlate well with other self-report screening tests of alcohol use (e.g., CAGE, Michigan Alcohol Screening Test), and are associated with biochemical measures of drinking (Bohn, Babor, & Kranzler, 1995).

Individual item scores range from 0 to 4, with the total score ranging from 0 to 40. Higher scores reflect increasing levels of problematic drinking. The severity of alcohol

use is classified into four categories: low risk (total score 0 – 7), mild/moderate risk (total score 8 – 15), moderate/high risk (total score 16 – 19), and very high risk (total score 20 – 40). A cutoff score of 8 is generally used as an indication of hazardous and harmful alcohol use, as well as possible alcohol dependence (Allen, et al., 1997; Reinert & Allen, 2002). For the purpose of this study, individuals with a high risk of alcohol abuse/dependence were precluded from entering the study, and as such, a cutoff of 16 was used.

Substance use

Substance use was assessed with the 10-item version of the Drug Abuse Screening Test ((DAST-10); see Appendix D) (Skinner, 1982). The DAST-10 is a brief face-valid self-report measure of problematic substance use other than alcohol that is commonly used for both research and clinical purposes. The DAST-10 has demonstrated acceptable internal consistency (Cronbach's alphas above .86 - .94) (Carey, Carey, & Chandra, 2003; Cocco & Carey, 1998), test-retest reliability (r = .71) (Cocco & Carey, 1998), and acceptable validity (Yudko, Lozhkina, & Fouts, 2007). All items are binary (yes/no), each valued at one point, yielding a total score of 0 – 10. Substance abuse severity can be classified according to the DAST-10 total score, with 0 representing no drug abuse problem, 1-2 a low level problem, 3-5 a moderate problem, 6-8 a substantial problem, and 9-10 a severe problem. A cutoff score of 3 is typically used to distinguish those with substance abuse/dependence of a clinical nature (Skinner, 1982). In an attempt to enhance generalizability of the participant sample, only those with DAST scores 6 and above were precluded from entering the study.

3.4 Treatment

3.4.1 Pharmacotherapy

3.4.1.1 Rationale for nicotine transdermal patch use

During the past 20 years, several nicotine replacement therapies (NRTs) have been marketed and evaluated as aids for smoking cessation including the nicotine patch, inhaler, nasal spray, gum, sublingual tablet, and lozenge. These treatments deliver nicotine systemically, providing pharmacological effects of nicotine similar to that obtained by smoking, and reducing physiological withdrawal symptoms (e.g., depressed mood, irritability, anxiety, headaches) (M. C. Fiore, Jorenby, Baker, & Kenford, 1992; Henningfield, 1995).

Several meta-analyses have clearly demonstrated that, in comparison to placebo, NRTs help smokers quit cigarettes (Capeda-Benito, 1993; M. C. Fiore, Smith, Jorenby, & Baker, 1994; Silagy, Mant, Fowler, & Lodge, 1994). Although all forms of NRTs are efficacious, transdermal nicotine patches have a number of advantages. It has been estimated that the clinical efficacy of nicotine transdermal systems is 60% greater than nicotine chewing gum (Gore & Chien, 1998). Nicotine patches also have a number of pharmacokinetic advantages. Nicotine transdermal patches can deliver nicotine directly to the systemic circulation via intact skin, thereby avoiding "first-pass" metabolism after oral administration (Gore & Chien, 1998). Additionally, contrary to nicotine gum, lozenges, nasal spray, and the inhaler – which produce an intensive fluctuation of nicotine plasma peaks and troughs – nicotine patches maintain a relatively steady-state plasma nicotine concentration profile (Gore & Chien, 1998). Therefore, with respect to

measuring the physiological effects of nicotine administration, the transdermal patch enables a more standardized dose by precluding idiosyncratic consumption characteristics such as chew frequency and oral placement which alters absorption rate of nicotine.

3.4.1.2 Clinical pharmacokinetics of the nicotine patch

Extensive studies have been conducted in order to delineate the drug release and skin permeation kinetics of nicotine transdermal patches. Results of all transdermal patch systems reveal that the delivery of nicotine is quite fast during the first 6-8 hours, and

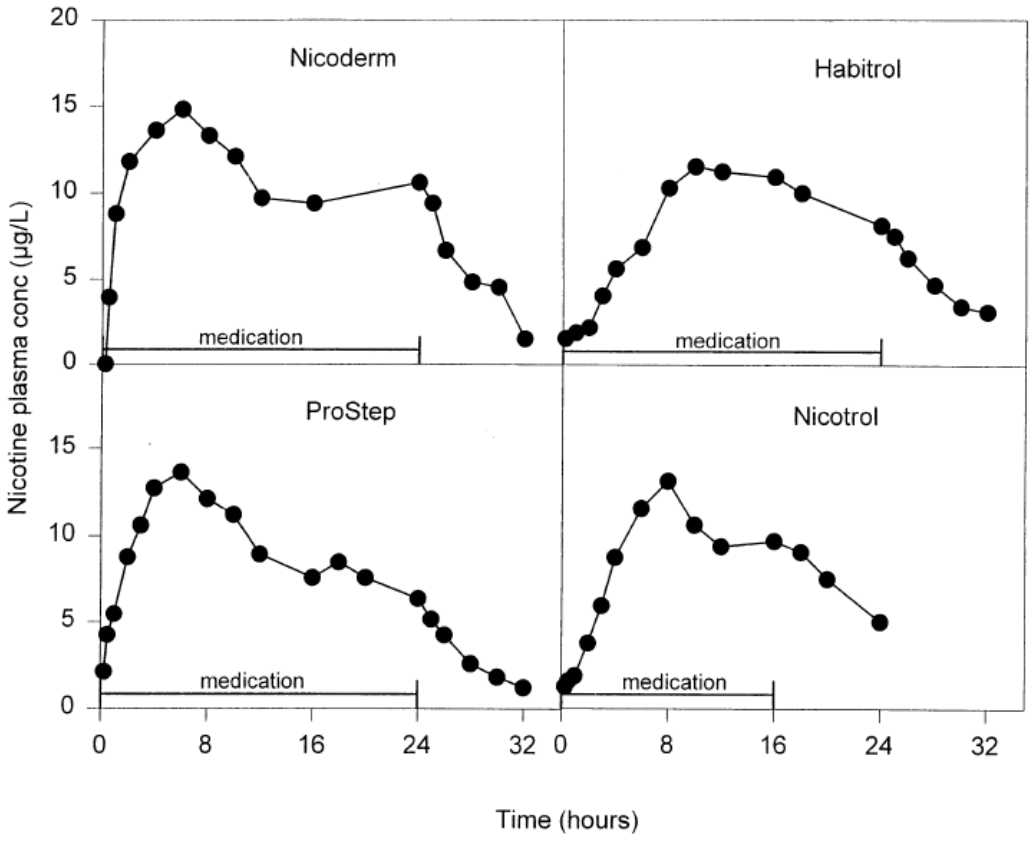

Figure 2: Comparative Pharmacokinetic Profiles of Nicotine in Humans After Single-Dose Application of Nicotine Transdermal Systems (n = 11–13).
Figure from Morgan and Cohen (1995).

then shifts to a lower rate of permeation at a steady state (Ho & Chien, 1993). Figure 2 delineates the single-dose pharmacokinetic profiles of 4 nicotine transdermal patch systems (Morgan & Cohen, 1995). It can be seen that three distinct phases exist: incline phase; plateau phase, which has a fairly steady plasma nicotine level; and decline phase, which follows the removal of the patch system. The administration of one patch, irrespective of brand, raises plasma nicotine concentration level to approximately 15μg/L. When a second nicotine patch is applied to a new skin site (after the removal of the initial patch), the gradual rise in nicotine levels during the incline phase overlaps with the declining plasma profile of the original patch, thus maintaining a virtually constant plasma concentration (Berner, 1992), without accumulation of nicotine over contiguous doses (Ross, Chan, Piraino, & John, 1991).

The pharmacokinetics of nicotine delivery via the transdermal patch is quite different from other delivery methods. As seen in Figure 3, nicotine nasal spray takes between 5 and 10 minutes to reach peak (Russell, Jarvis, Feyerabend, & Ferno, 1983), demonstrating a similar rate of action as smoking cigarettes (Benowitz, Porchet, Sheiner, & Jacob, 1988). However, plasma levels of nicotine delivered nasally drop rapidly, yielding a highly fluctuating profile. Nicotine gum produces a more stable plasma profile; however peak plasma concentration is lower compared to other NRTs (Tutka, Mosiewicz, & Wielosz, 2005), and many patients report gastrointestinal upset (Henningfield, 1995).

Considering the literature supporting nicotine patch efficacy and tolerability, as well as the ease of use (administered once per day compared to ad lib), I believed that

administering the nicotine patch, compared to other NRTs, would produce the highest abstinence rates.

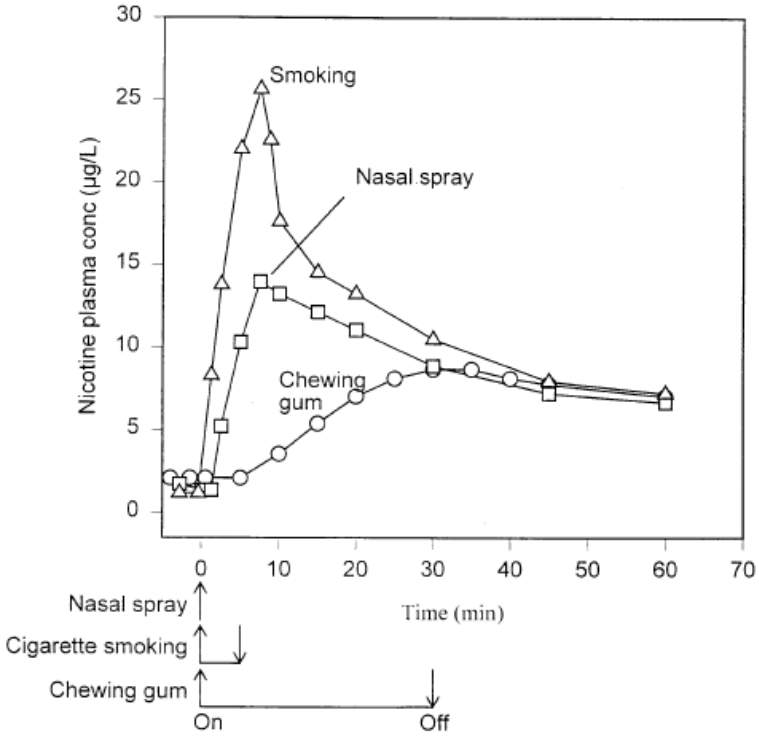

Figure 3. Comparative Pharmacokinetic Profiles of Nicotine from Different Nicotine Products. Keys: (△) Cigarette (1.97 mg); (□) Nasal spray (2-mg dose); (○) Nicorette® chewing gum (2-mg dose). Nicotine: 1 nmol/L ≈ 0.16 ng/mL. Modified from Russell et al. (1983).

3.4.1.3 Nicotine patch dose and regimen

Participants were given an 8-week nicotine transdermal patch treatment (Habitrol®, Novartis Consumer Health Inc., Summit, NJ, USA) administered in a step-down fashion (21-mg, weeks 1-4; 14-mg, weeks 5-6; 7-mg, weeks 7-8). The patch was applied once daily, usually at the same time each day (typically upon wakening), and was

worn continuously for 24 hours. The 21-mg patch was administered at the beginning of treatment because this dose is the most appropriate for heavy smokers (>15 cigarettes/day). Changes in treatment length (extension or reduction) at the request of a participant were permitted. In cases where enrolled participants reported (at their initial visit) smoking less than the minimum requirement (15 cigarettes/day), treatment regimens were tailored accordingly, under the supervision of a consulting pharmacist.

3.4.2 Adjunctive counseling

3.4.2.1 Overview of adjunctive counseling

Research indicates that combining in-person and/or telephone counseling with NRT significantly enhances quit rates (M. Fiore, et al., 2000; Macleod, Charles, Arnaldi, & Adams, 2003). Adjunctive counseling may enhance smoking cessation medications by helping smokers understand NRTs with respect to their limitations, mechanisms of action, safe use, and adjustment to medication termination (M. Fiore, et al., 2000; Perkins, Conklin, & Levine, 2007). Counseling also can serve as an important reinforcement of a smoker's motivation for quitting, thereby reducing relapse.

3.4.2.2 Adjunctive counseling components

Individual counseling was developed based upon the tobacco use and dependence clinical practice guidelines (M. Fiore, et al., 2000) and the protocols of the National Cancer Institute (Glynn & Manley, 1990). Individual counseling was intensive and emphasized brief assessment, psycho-education, behavioral modification, and cognitive intervention. Assessment included examining a participant's level of motivation and

confidence to quit, reasons for quitting, current nicotine dependence level, daily smoking patterns (overall frequency, location, time-specific intake patterns), and triggers/cues for smoking. Psycho-education entailed discussing the medical risks of continued smoking, medical consequences of fading cigarette intake versus complete cessation, the relationship between smoking and weight/diet, positive predictors of smoking success, physiological and psychological aspects of nicotine dependence, and rationale for and education on the safe use of the nicotine transdermal patch. Several behavioral interventions were utilized such as self-monitoring, trigger reduction (removal of smoking related cues such as ashtrays, lighters, empty cigarette boxes, and specific environments), changing daily routines, increasing exercise and sleep, nutritional recommendations, and progressive muscle relaxation techniques. Cognitive interventions included identifying and altering maladaptive beliefs regarding cigarette smoking.

3.4.2.3 Adjunctive counseling duration and frequency

The first in-person counseling session, which occurred during a participant's first visit to the laboratory, lasted 45 minutes. The second in-person counseling session lasted 30 minutes and occurred during the second experimental session. Handouts were given which entailed many of the psycho-education components described above. Participants also received a minimum of 10 weekly telephone counseling sessions each lasting 10 minutes in duration. These phone sessions targeted topics that were relevant to the individual's place in the quitting process. In-person counseling interventions were conducted by a trained psychology graduate student. Telephone counseling was performed by a trained research assistant supervised by the primary investigator.

3.5 Procedure

3.5.1 Overview of procedure

Prospective study participants were screened by telephone to determine their eligibility to enter the study (see Section 3.2.2 detailing inclusion/exclusion criteria). Eligible participants were asked to abstain from caffeine and alcohol for 2 hours prior to each experimental condition. During the initial telephone screening, a quit date was set, which corresponded to the day after their first experimental session. Participants were asked to not reduce their smoking frequency from the time of initial screening to the time of their first appointment, as research indicates no differential treatment outcome in successful cessation as a function of smoking as usual versus cutting down on cigarette intake prior to nicotine replacement therapy use (Günther, Gritsch, & Meise, 1992; Hughes, 2000). Additionally, it was important for participants to smoke as usual leading up to their first session in order to ensure an accurate assessment of baseline sexual functioning.

Participants were not asked to refrain from smoking during the day of their initial assessment, and therefore they entered the laboratory at their preferred nicotine level. This was in order to rule out confounding effects of withdrawal symptoms on sexual functioning. Additionally, participants were not allowed to smoke during any experimental session. Considering that acute nicotine intake significantly inhibits sexual arousal in nonsmokers (Harte & Meston, 2008a), it may be possible that smoking-induced ED is largely a result of acute deleterious effects of nicotine and/or tobacco smoke on sexual function, irrespective of smoking history. I believed that having

participants smoke prior to entering the laboratory (corresponding to approximately 1 hour from nicotine administration to physiological assessment of sexual arousal) would enable a more accurate assessment of "baseline" erectile functioning, thereby precluding withdrawal effects and nicotine-induced acute effects.

All participants were tested individually while seated in a comfortable armchair within a dimly lighted private, internally locked testing room with a television monitor approximately 10 feet away. An intercom system between the participant and the experimenter rooms allowed for communication with participants at all times. Only a male experimenter tested male participants. The protocol was approved by the University of Texas at Austin Institutional Review Board.

3.5.2 Procedure

Visit 1 – Pre-treatment (baseline assessment while smoking)

The researcher explained the experimental procedure and showed the participant the laboratory and the measurement devices used to assess subjective and physiological sexual arousal. Participants then read a consent form, which contained information with respect to the nature, purpose, potential risks, and contact information for individuals responsible for the study. The informed consent also included specific information about how data would be kept confidential, the safety of the physiological equipment, and the general study procedure. Participants were asked to sign one copy for the researcher's records, and keep another copy for their records. Each participant was also asked to sign a contract stating that he was committed to completing all experimental sessions, regardless of his smoking status.

Visit Number		1			2					*				3
Study Day	**Screening**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**57**	**64**	**71**	**78**	**85**
Screening Measures														
Alcohol Use (DAST)	X													X
Susbstance Use (AUDIT)	X													X
Kinsey Sexual Orientation Scale	X													
Smoking History	X	X												
Medical History	X	X												
Primary Outcome Measures														
Physiological sexual arousal		X			X									X
Continuous self-reported sexual arousal		X			X									X
Self-reported sexual functioning (IIEF)		X			X									X
Cardiovascular Measures														
Blood pressure		X			X									X
Heart rate		X			X									X
Anthropomorphic Measures														
Height		X												X
Weight		X			X									X
Moderating Variables														
Affect (PANAS)		X			X									X
Nicotine Dependence (FTND)		X												
Nicotine patch compliance**			X	X	X	X	X	X	X	X	X	X	X	X
Intra- and post-treatment tobacco use**			X	X	X	X	X	X	X	X	X	X	X	X
Safety Determinations														
SAFTEE					X					X				

Table 3. Time Events Chart Listing all Measures and Occasions for their Administration.

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test; DAST-10 = Drug Abuse Screening Test, 10-item version; FTND = Fagerström Test of Nicotine Dependence; IIEF = International Index of Erectile Functioning; PANAS = Positive and Negative Affect Schedule; SAFTEE = Systematic Assessment for Treatment Emergent Events.

*The SAFTEE was administered via telephone, thereby precluding a visit to the laboratory.

**Nicotine patch compliance, as well as smoking and/or NRT use during patch treatment and post-treatment, was assessed via telephone.

After giving consent, the participant's height and weight were measured, and his heart rate and systolic and diastolic blood pressures were assessed. Participants were then questioned on their smoking history and current smoking patterns. They were then asked to complete a battery of questionnaires in privacy (see Table 3 for a detailed time events chart listing the measures and occasions for their administration). Participants also provided a saliva sample and they were spuriously informed that all samples would be assayed for salivary nicotine content. This was to help ensure valid self-reporting of cigarette consumption.

After participants completed the survey packet, they were instructed on how to fit the penile plethysmograph, and how to use the subjective sexual arousal device. The electrocardiograph leads were also attached. Participants were then randomized to view 1 of 3 films. All visual presentations started with word "relax" presented on the screen for 1 minute. This was followed by a nonsexual neutral segment (3 minutes consisting of a documentary film) after which an erotic video segment (8 minutes consisting of a heterosexual couple engaging in petting, oral sex, and sexual intercourse) was immediately presented. These films have previously been shown to reliably elicit physiological and subjective sexual arousal in men (Harte & Meston, 2008a). The sequences of films differed only in the content of the neutral and erotic films, and these films were counterbalanced across subjects. During film presentation, participants were asked to continuously monitor their level of subjective sexual arousal using a hand-controlled device positioned to the side of the chair in which they were seated.

Immediately following the erotic film, participants were instructed via the intercom system to remove the plethysmograph and remove the electrocardiograph leads. Participants were given 28 high dose patches (21-mg, 24-hour release; to be worn once daily for 4 weeks), and were asked to start nicotine replacement therapy the following morning. Participants were given detailed instructions on proper and safe use of the patch, and were also given handouts which included information on how to maximize their smoking cessation effectiveness. Finally, participants received cognitive-behavioral counseling, and weekly 10-minute phone counseling sessions were scheduled. The entire session lasted 2 hours.

Visit 2 – Treatment (assessment while using the nicotine transdermal patch)

Participants returned to the laboratory for their second visit, during the fourth week of their 21-mg nicotine transdermal patch treatment. The test session was identical to visit 1 described above, with the exception that they will not be assessed anthropometrically (see Table 3). Pharmacotherapy-related side effects were assessed, and participants were given fourteen 14-mg patches (24-hour release; to be worn once per day for 2 weeks), and fourteen 7-mg patches (24-hour release; to be worn once per day for 2 weeks) to be used for the remaining 4 weeks of pharmacotherapy. Participants were asked to start the 14-mg patch the following morning after they were finished with their last 21-mg patch. Participants continued to be contacted once weekly to assess patch compliance and intra-treatment tobacco use, as well as participate in 10-minute phone counseling. The entire session lasted 1.5 hours.

End-treatment safety check

Side effects during weeks 5 through 8 of the nicotine patch regimen were assessed again at the completion of the patch treatment via telephone. Participants continued to be contacted once weekly for 10-minute phone counseling sessions.

Visit 3 – Follow-up (4 week post-treatment assessment)

Four weeks after cessation of the nicotine patch, participants were reevaluated. Specifically, their height and weight were reassessed, as well as their self-report measures of sexual functioning and mood (see Table 3). Participants again provided saliva samples, and were assessed psychophysiologically as described in visits 1 and 2. Participants were debriefed and given an opportunity to ask any questions relating to the study. They were then provided $30 in cash for study completion, and were mailed a detailed report (see Appendix H) of their laboratory assessments within one week. The session lasted 1 hour.

CHAPTER 4: DATA ANALYSIS

4.1 Data reduction

With respect to physiological sexual arousal, movement artifacts—defined as clear spikes >5 mm within an otherwise smooth curve (George, et al., 2006)—were deleted. The remaining raw data were digitally transformed into millimeters of circumference change. Initial physiological and continuous subjective sexual arousal scores for each session were computed by averaging all data points within 10-second epochs, and then all epochs within the neutral (18 epochs) and erotic films (48 epochs) were separately averaged. For physiological sexual arousal, change scores were calculated by subtracting the mean during the neutral film from the mean during the erotic film. Percent change (from the neutral film to the erotic film) was calculated for both physiological and continuous subjective sexual arousal. Heart rates during the film presentation were averaged across the neutral and erotic films, yielding a total of three heart rate measures (one prior to the film sequence, and two during the film sequence) for each participant per experimental condition. With respect to self-reported sexual function, participants reporting an erectile function score of less than or equal to 25 were considered to be experiencing erectile dysfunction of a clinical nature.

4.2 Defining treatment outcome groups

Efficacy of smoking cessation was evaluated with the use of a 1-week point prevalence abstinence rate at follow-up (week 12). Participants were classified as being totally abstinent if they reported smoking zero cigarettes during the previous seven days,

whereas individuals reporting smoking 1-20 cigarettes during the prior seven days were classified as being partially abstinent. Men smoking more than 20 cigarettes were considered relapsed. Because there were no differences between completely and partially abstinent men for any of the outcome measures (all *p*s > .05), these groups were combined for the initial analyses involving the subgroup of successful quitters only.

For the intent-to-treat (ITT) analyses, which included all participants, a more stringent classification was adopted: participants reporting zero cigarettes during the prior 7 days at follow-up were considered successful quitters, whereas individuals reporting 1 or more cigarettes were classified as unsuccessful quitters (relapsers). With respect to treatment efficacy data, the above stringent classification was used.

4.3 Statistical analyses

4.3.1 Overview

All dependent variables were checked for normality using Shapiro–Wilk tests with an alpha of $p < .05$ denoting a normality violation. Variables that were not normally distributed were log transformed. All analyses were performed using SPSS statistical software version 18.0 (SPSS Inc., Chicago, IL, USA). A two-tailed alpha of $p < .05$ was considered statistically significant for all analyses. Effect sizes (i.e., Cohen's *d,* Pearson *r*, Cramér's φ) were reported when comparing two groups. Measures of variance, such as η^2 and R^2, were reported when comparing more than two groups and magnitude of association, respectively. All variances and effect sizes were calculated according to the guidelines proposed by Cohen (1988).

4.3.2 Statistical power considerations

A priori power analyses for a 3 (experimental session) × 2 (group: successful quitter vs. relapser) repeated measures analysis of variance (ANOVA) design, with a moderate effect size (f = .32) and a two-tailed alpha set at .05, suggested that 18 participants in each group were necessary at each time point in order to have power of 0.80 to detect group-specific across-session differences. The a priori effect size of .32 was taken from a previous study (Harte & Meston, 2008a) examining acute effects of nicotine administration on sexual arousal using the same methods and instrumentation as the proposed study. Additionally, a priori power analyses indicated that a total sample size of 54 participants was necessary in order to adequately assess between-group differences. To ensure sufficient power, 65 participants were enrolled.

4.3.3 Handling missing data

All initial analyses were conducted on the subgroup of successful quitters only (complete abstainers and partial abstainers combined). Across-session changes were assessed using list-wise deletion, as well as with the traditional last observation carried forward (LOCF) technique, and full information maximum likelihood (FIML) estimation (Little & Rubin, 2002). The FIML approach was used with the expectation maximization (EM) algorithm, which estimates missing values iteratively by case-wise maximizing the likelihood of the observed data in the dataset (Wothke, 2000). This technique was employed because this approach produces more accurate parameter estimates than list-wise deletion and LOCF (Enders, 2001; Enders & Bandalos, 2001; J.L. Schafer & Graham, 2002).

Additionally, ITT analyses were conducted for all participants (successful quitters and relapsers) using FIML. Missing values (for session 2 and 3) for each primary outcome variables were successively estimated using several characteristics as predictors such as age, pack years, baseline smoking frequency, erectile dysfunction status, drug and alcohol severity, dropout status, as well as each corresponding baseline primary outcome value. Additionally, the total number of cigarettes smoked throughout the study, the total number of days a participant wore the patch, and the number of cigarettes smoked during week 12 were estimated in a similar fashion. For the ITT analyses, group status (successful quitter, relapser) was based on these imputed values.

4.3.4 Tests of potential confounding variables

For the initial analyses on the subgroup of successful quitters, potential demographic (age, pack years), physical (BMI, flaccid penile circumference[*]), clinical (erectile functioning as per the IIEF, alcohol and substance use), and protocol-related (total cigarettes smoked during study, total days of patch use) confounding variables were entered into a stepwise multiple regression analysis for each outcome variable for each type of missing data approach (i.e., list-wise deletion, LOCF, FIML). For the list-wise approach, the only variable that reached significance was total cigarettes smoked throughout the study with respect to the intercourse satisfaction subscale of the IIEF ($p <$ .01). For LOCF and FIML, total cigarettes smoked throughout the study, age, and pack years were entered as covariates in all analyses.

[*]This was entered as a possible covariate because differences in individual flaccid penis size cause differential circumferential changes during sexual arousal (Jamison & Gebhard, 1988).

For the ITT analyses, pack years, total cigarettes smoked throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at visit 2 (smoke-free, relapsed) were entered as covariates in all analyses.

4.3.5 Validity check for the audiovisual manipulation

In order to ensure that the erotic stimuli facilitated sexual arousal, two separate 2 (Film segment: neutral vs. erotic) × 3 (Film sequence (i.e., which of the 3 erotic films were shown during the first experimental session)) repeated measures ANOVAs were conducted with both physiological sexual arousal and continuous self-reported sexual arousal as dependent measures. There was an overall main effect of film for both physiological ($F(1,62) = 98.04$, $p < .001$, $\eta^2 = .61$) and self-reported ($F(1,62) = 381.51$, $p < .001$, $\eta^2 = .86$) sexual arousal, indicating that the audiovisual stimuli were sufficient to elicit reliable sexual arousal responses. The lack of a film segment by film sequence interaction for either physiological ($p = .97$) or subjective ($p = .65$) sexual arousal indicated that all films induced sexual arousal to a similar degree.

4.3.6 Tests of major study hypotheses

Aim 1: To investigate within- and between-group changes in physiological sexual arousal. Separate repeated measures ANCOVAs, with time (baseline, pre-treatment, follow-up) as a within-subjects factor, were performed on each of the physiological sexual arousal indices (raw change and percent increase in penile tumescence, maximum arousal, percent change to maximum arousal, latency to maximum arousal, and slope to maximum erection) among successful quitters. Greenhouse-Geisser corrected

significance values were reported when the sphericity assumption was not met. Planned comparison paired sample *t*-tests for adjusted cell means were used to assess across-session differences.

With respect to the ITT analyses, general linear modeling was used as the primary analytic approach to compare the two groups at each time point for all outcome measures. Specifically, a series of univariate 3×2 repeated measures ANCOVA models were employed. This approach enabled the modeling of outcome measures as a function of time of assessment (within subjects), treatment effects (between subjects), and covariate characteristics. For these analyses, the interaction effect of treatment×time was of primary interest. In cases where the overall interaction term was statistically significant, planned comparison *F*-tests for adjusted cell means were used to assess between-group differences at each time point.

Aim 2: To investigate within- and between-group changes in continuous subjective sexual arousal. Analyses were similar to those used in Aim 1, with repeated measures ANCOVAs, with time as a within-subjects factor, performed on each of the continuous subjective sexual arousal variables (percent change in sexual arousal, latency to maximum arousal, and slope to maximum arousal) among successful quitters. Planned comparison paired sample *t*-tests for adjusted cell means were used to assess across-session differences. Intention-to-treat analyses were conducted similar to those in Aim 1.

Aim 3: To investigate within- and between-group changes in self-reported sexual function. Analyses were similar to those used in Aims 1 and 2, with repeated measures ANCOVAs, with time as a within-subjects factor, performed on 6 of 7 sexual function

variables (erectile function, orgasmic function, sexual desire, intercourse satisfaction, overall satisfaction, and overall sexual functioning) among successful quitters. Paired sample *t*-tests for adjusted cell means were used to assess across-session differences. To examine across-session changes in proportion of men with ED, Pearson χ^2 tests were used.

Analyses on the intent-to-treat sample were conducted similar to those in Aim 1. Additionally, multivariate logistic regression analyses were used to examine the association between quitting smoking and erectile dysfunction status at mid-treatment and follow-up. Variables were examined using the Wald test and adjusted odds ratios with their 95%confidence intervals were calculated.

4.3.7 Tests of moderator hypotheses

Whether subjective ratings of affect covaried with the three outcome measures (physiological sexual arousal, continuous self-reported sexual arousal, self-reported sexual function) were explored for both successful quitters and unsuccessful quitters separately. Difference scores between the first and last session were separately derived within participants for each outcome measure, as well as for positive and negative affect scores. These sets of difference scores were then entered into separate regression models.

4.3.8 Additional analyses

A series of 3 (session: baseline, pre-treatment, follow-up) ×2 (group: successful quitter, unsuccessful quitter) repeated measures ANCOVA models were employed to examine the effects of smoking cessation on systolic and diastolic blood pressure scores,

and on BMI. Resting heart rates were analyzed with a 3 (session: baseline, pre-treatment, follow-up) × 2 (group: successful quitter, unsuccessful quitter) repeated measures ANOVA. In the case where the overall interaction term was statistically significant, planned comparison *F*-tests for adjusted cell means were used to assess between-group differences at each time point.

Differences in baseline characteristics between treatment completers and dropouts, as well as between successful and unsuccessful quitters, were compared with *t* tests or Pearson χ^2 tests, as appropriate. Fisher's Exact tests were used in cases with low cell counts. A Pearson product moment correlation coefficient was used to quantify the relation between physiological and continuous self-reported sexual arousal for each experimental session.

CHAPTER 5: RESULTS

5.1 Participant characteristics

Two hundred twenty-eight men completed the initial telephone screening. Of these individuals, 116 were ineligible, 9 declined to participate, and 9 were unable to be contacted further in order to enroll. Of the 112 men who met inclusion criteria, 47 did not show for their initial evaluation, resulting in a final sample of 65 participants. The dropout rate was 28% after the initial visit, and 49% after the second visit, resulting in 51% who completed the study (see Figure 4 for participant flow).

The total sample had a mean age of 39 years (*SD* = 10.76; range, 23-58), was predominantly White (86%), reported an average of 15 years of education (*SD* = 2.23; range, 12-22), and reported a mean of approximately 22 pack-years (*SD* = 16.17; range, 2-77). Participants reported a mean age of smoking onset of 17 years (*SD* = 4.56; range, 8-40), and were smoking an average of 22 cigarettes per day (*SD* = 7.89; range, 12-40), and were highly addicted to tobacco (FTND total score = 5.45; *SD* = 1.97; range 1-10). The sample had a mean IIEF erectile function score and a mean IIEF total score of 26.7 (*SD* = 4.88; range, 2-30) and 62.3 (*SD* = 10.15; range, 20-75), respectively, and approximately 29% of these participants had ED according to IIEF established standards. Mean scores for other domains of sexual functioning as per the IIEF were as follows: orgasmic function (*M* = 9.0; *SD* = 1.48), sexual desire (*M* = 7.2; *SD* = 1.69), intercourse satisfaction (*M* = 11.7; *SD* = 2.81), and overall satisfaction (*M* = 7.7; *SD* = 1.89). Seventeen men reported taking medications, the majority of which were allergy related. Characteristics of the participant sample are presented in Table 4.

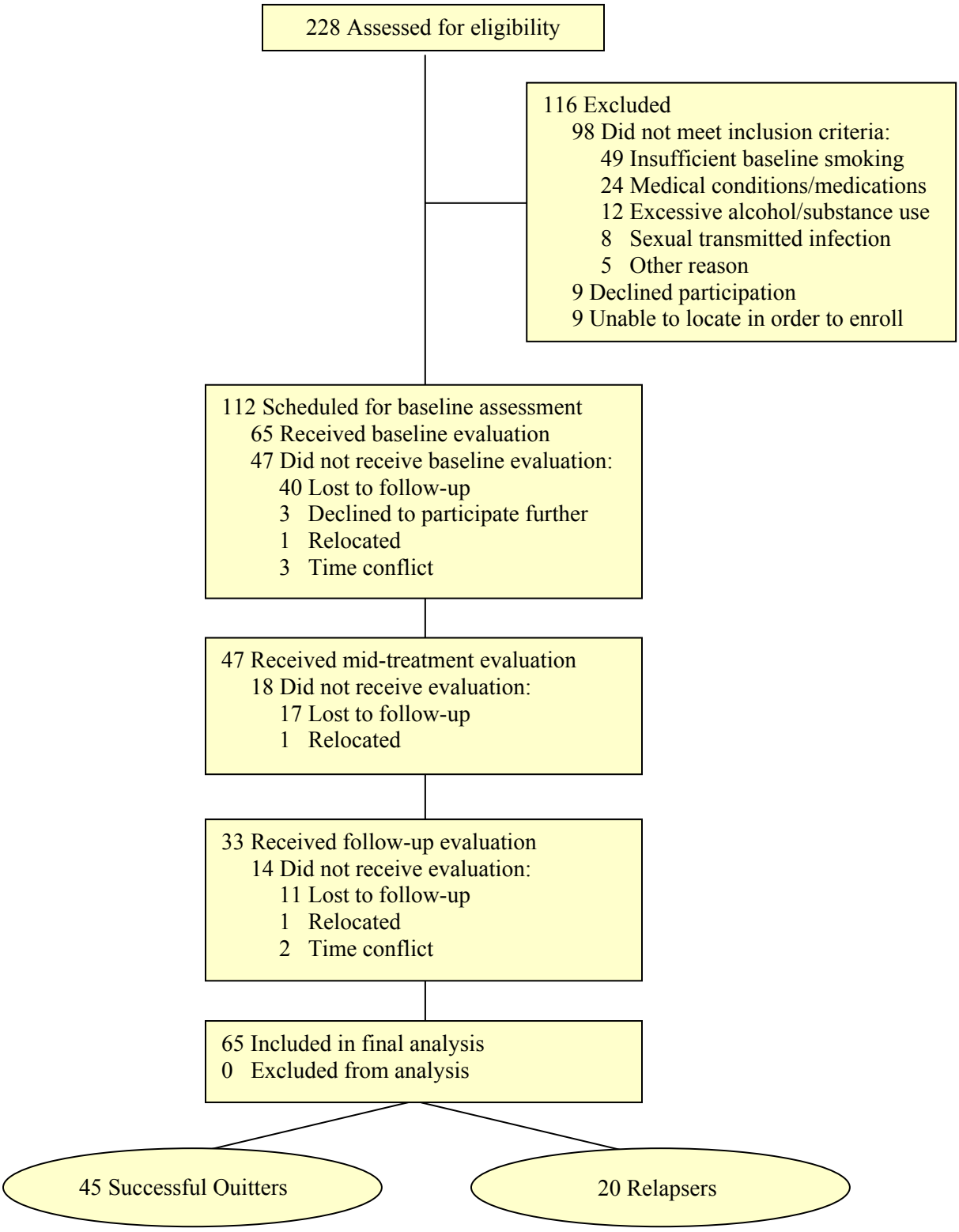

Figure 4. Participant Flow.

Characteristic	Successful quitters (*n* = 20)		Unsuccessful quitters (*n* = 45)		*P* value
	Mean (*SD*)	*n* (%)	Mean (*SD*)	*n* (%)	
Demographics					
Age (years)*	34.9 (9.65)		40.4 (10.9)		**.06**
Education (years)†	15.5 (2.04)		14.4 (2.25)		**.07**
Ethnicity					
White		19 (95.0)		37 (82.2)	
African-American		0 (0.0)		3 (6.7)	
Latino/a		0 (0.0)		3 (6.7)	.19
Asian		0 (0.0)		2 (4.4)	
Other		1 (5.0)		0 (0.0)	
Income (US dollars)					
< 25,000		6 (30.0)		7 (15.6)	
25,000 - 49,999		6 (30.0)		18 (40.0)	
50,000 - 74,999		6 (30.0)		9 (20.0)	.45
75,000 - 99,000		2 (10.0)		6 (13.3)	
≥ 100,000		0 (0.0)		5 (11.1)	
Marital status					
Single		12 (60.0)		15 (33.3)	
Married		4 (20.0)		18 (40.0)	
Common Law		1 (5.0)		3 (6.7)	.53
Divorced		3 (15.0)		8 (17.8)	
Widowed		0 (0.0)		1 (2.2)	
BMI (kg/m^2)	25.9 (3.67)		26.2 (4.81)		.80
Screening measures					
AUDIT score	6.9 (3.13)		4.1 (3.18)		**<.01**
DAST-10 score	.7 (.98)		.6 (.78)		.66

Table 4. Demographics of the Participant Sample.

Characteristic	Successful quitters		Unsuccessful quitters		
	Mean (*SD*)	*n* (%)	Mean (*SD*)	*n* (%)	*P* value
Smoking characteristics					
Age of onset (years)*	16.1 (2.37)		16.8 (5.3)		.57
Smoking duration (years)*	17.9 (10.03)		22.6 (11.4)		.12
Pack years	18.2 (14.02)		23.1 (16.9)		.26
Current smoking frequency (cigs/day)*	19.0 (5.09)		22.8 (8.66)		**.07**
Nicotine dependence*‡	5.4 (1.84)		5.5 (2.04)		.78
Number of quit attempts*	3.4 (2.78)		3.5 (2.66)		.81
Smoking partner¥		6 (30.0)		17 (39.5)	.46
Motivation level to quit smoking*	8.4 (1.09)		8.5 (1.11)		.70
Confidence level to quit smoking*	7.3 (1.52)		7.5 (1.93)		.68
Sexual functioning¶					
Erectile function	27.0 (4.75)		26.5 (5.19)		.72
Orgasmic function	8.7 (1.87)		9.0 (1.42)		.45
Sexual desire	6.8 (1.52)		7.4 (1.74)		.13
Intercourse satisfaction	11.9 (2.13)		11.6 (3.08)		.67
Overall satisfaction	7.9 (1.76)		7.6 (1.95)		.63
Overall sexual functioning (total score)	62.2 (9.97)		62.2 (10.60)		.99
Erectile dysfunction**		4 (20.0)		15 (33.3)	.28

Table 4 (cont). Demographics of the Participant Sample.

Abbreviations: AUDIT= Alcohol Use Disorders Identification Test; BMI = Body mass index; DAST-10 = Drug Abuse Screening Test, 10-item version.

*Data were missing for 1 participant.

†Data were missing for 3 participants.

‡As per the Fagerström Test of Nicotine Dependence.

¥ Data were missing for 2 participants.

¶Measured on a scale from 0-10, with higher numbers representing higher levels of motivation/confidence.

**As per the International Index of Erectile Functioning (IIEF).

***According to the IIEF erectile functioning cutoff score of 25

The two subgroups of smokers did not differ significantly on the majority of socio-demographic and smoking characteristics, with the exception of age, education, and current smoking frequency. Specifically, unsuccessful quitters showed a statistical trend toward fewer years of education ($t(63) = 1.87$, $p = .07$; $d = .23$), increased age ($t(63) = 1.95$, $p = .06$; $d = .24$), and higher number of cigarettes smoked daily ($t(63) = 1.83$, $p = .07$; $d = .23$). The only other variable on which groups differed was baseline drinking severity, with unsuccessful quitters reporting significantly less alcohol use compared to successful quitters ($t(63) = 3.24$, $p < .01$; $d = .40$).

Analyses comparing treatment completers and dropouts revealed that these groups did not differ with respect to baseline measures of alcohol and substance use, sexual functioning, smoking and nicotine dependence, or motivation and confidence levels regarding quitting. The only variables that distinguished completers and dropouts were education and race. Specifically, those who dropped out reported less years of education ($t(60) = 2.34$, $p = .02$; $d = .60$), and were more likely to be non-White ($\chi^2(1) = 6.57$, $p = .01$; $\varphi = .32$). No other demographic characteristics distinguished between completers and dropouts (all ps $> .05$).

5.2 Treatment efficacy

Of the 65 men enrolled in the study, 7 reported relatively low nicotine dependence and required a non-standardized patch-treatment plan. Of these individuals, 6 received the 14-mg patch for 4 weeks followed by 4 weeks of the 7-mg patch, while 1 individual received 6 weeks of the 7-mg patch only. All other men received the standard treatment regimen.

Thirty-five percent (23 of 65) and 69 percent (45 of 65) of men were considered relapsed at mid-treatment and follow-up, respectively. The total sample of participants reported wearing the patch an average of 29 days and reported smoking an average of 281 cigarettes throughout the 12-week study. Successful quitters, compared to those that relapsed, reported smoking significantly less cigarettes ($t(63) = -6.45$, $p < .001$; $d = .80$) and reported a significantly higher number of days using the patch ($t(63) = 1.97$, $p = .05$; $d = .27$). Seven men reported supplementing the patch with other forms of NRT (nicotine gum, $n = 4$; nicotine lozenge, $n = 3$). The mean number of non-patch NRT usages was 55 ($SD = 55.95$; range, 1-140).

Adverse events were rare and occurred in 29% of participants while using the 21-mg patch and in 7% of participants toward the end of treatment (while using the 7-mg patch). On average, participants reported a total of .6 adverse events at mid-treatment and .2 adverse events at end-treatment. These included headache ($n = 2$), dizziness ($n = 1$), insomnia ($n = 3$), and itching ($n = 7$), and a rash ($n = 2$). All symptoms were reported as being minimal to mild in severity, and no adverse events affected the course of nicotine patch treatment.

5.3 Results of major study hypotheses among the subgroup of successful quitters

5.3.1 Analyses of physiological sexual arousal

With respect to participants that produced reliable physiological sexual arousal responses ($n = 21$), there were significant across-session differences for all six physiological sexual arousal outcome variables. Specifically, there was a significant main effect of time for raw change in erectile tumescence ($F(2,40) = 4.61$, $p = .02$, $\eta^2 = .19$)

(see Figure 5), percent change in penile tumescence ($F(2,40) = 3.13$, $p = .05$, $\eta^2 = .12$) (see Figure 6), raw change in maximum erectile response ($F(2,40) = 6.14$, $p < .01$, $\eta^2 = .24$) (see Figure 7), percent change in maximum erectile response ($F(2,40) = 8.60$, $p = .001$, $\eta^2 = .26$) (see Figure 8), latency to reach maximum arousal ($F(2,40) = 5.69$, $p = .01$, $\eta^2 = .22$) (see Figure 9), and rate of onset to maximum erection ($F(2,40) = 6.35$, $p = .01$, $\eta^2 = .24$) (see Figure 10).

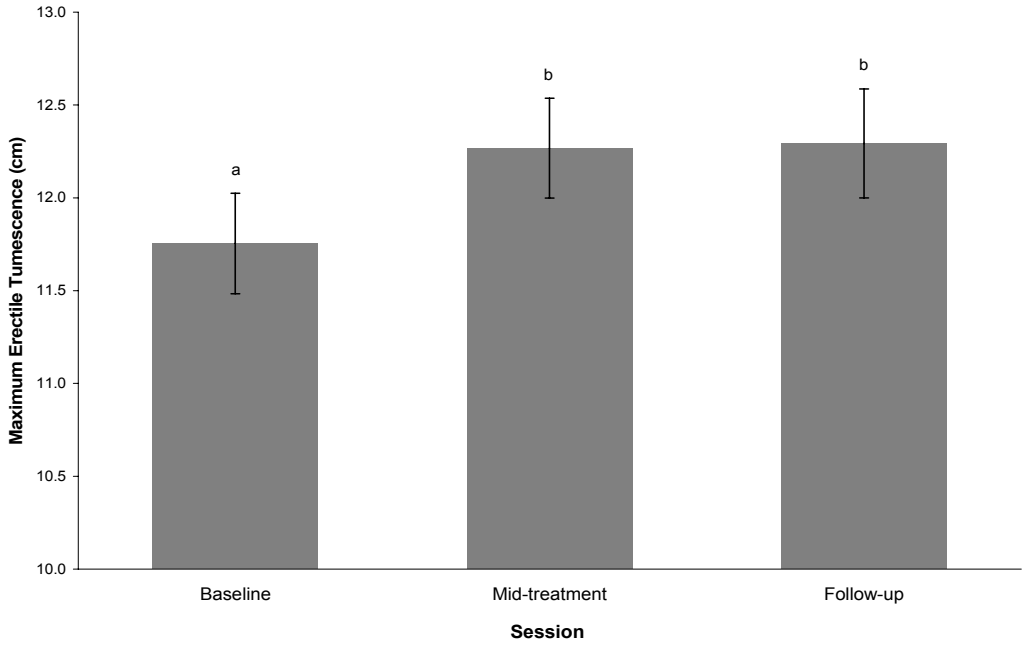

Figure 5. Raw Changes in Erectile Tumescence for Successful Quitters as a Function of Time. Bars represent mean within-session erectile tumescence change scores (mean tumescence during erotic stimulus minus mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

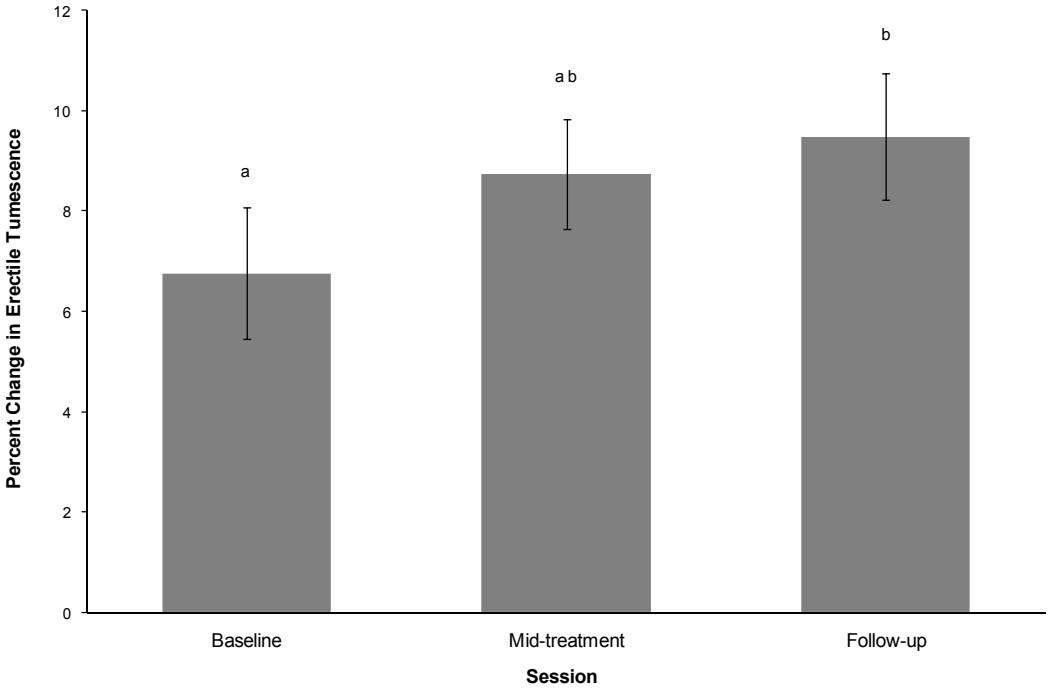

Figure 6. Percent Changes in Erectile Tumescence for Successful Quitters as a Function of Time. Bars represent mean within-session erectile tumescence percent change scores (mean tumescence during erotic stimulus minus mean tumescence during neutral stimulus divided by mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

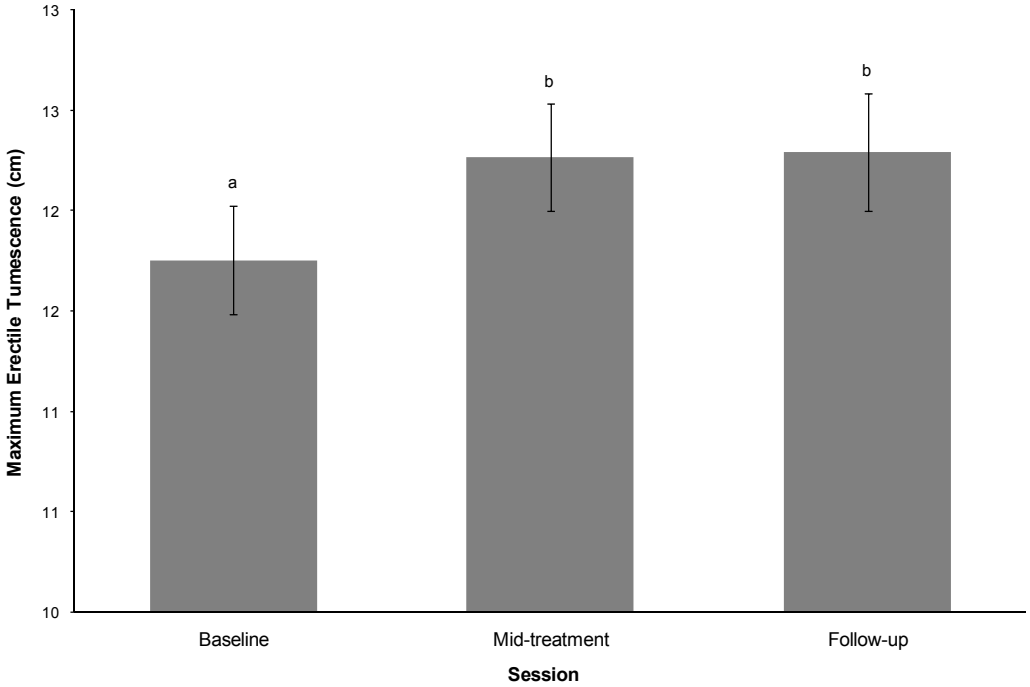

Figure 7. Raw Changes in Maximum Erectile Response for Successful Quitters as a Function of Time. Bars represent mean maximum erectile tumescence scores. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

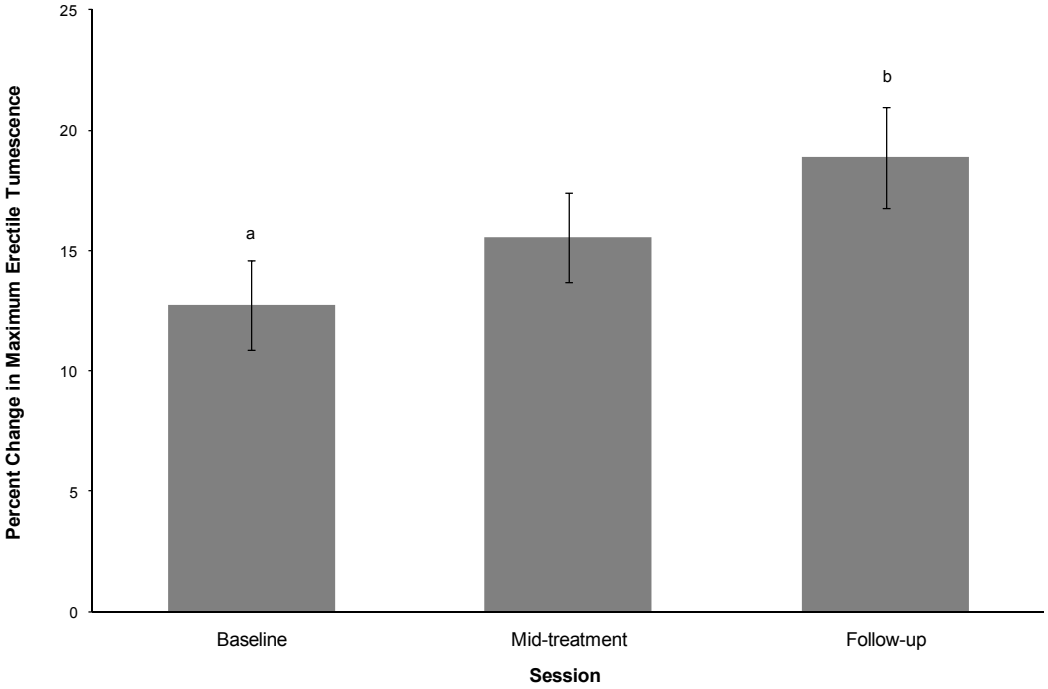

Figure 8. Percent Changes in Maximum Erectile Response for Successful Quitters as a Function of Time. Bars represent mean within-session percent changes in maximum erectile tumescence scores (maximum tumescence during erotic stimulus minus mean tumescence during neutral stimulus divided by mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

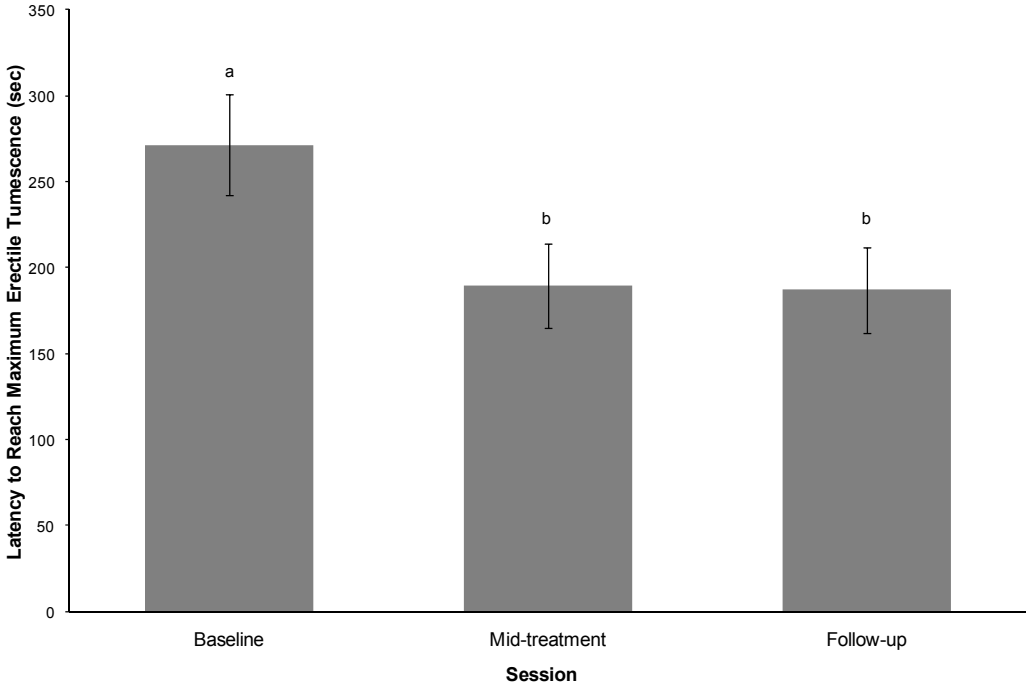

Figure 9. Latency to Reach Maximum Erection for Successful Quitters as a Function of Time. Bars represent mean latencies to reach maximum erectile response. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

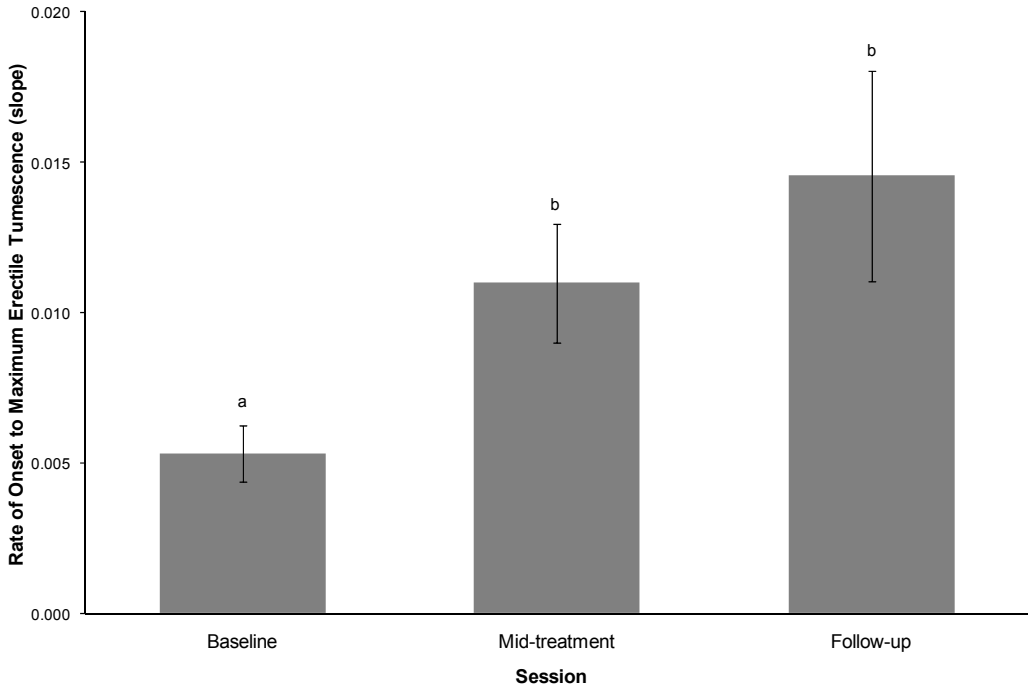

Figure10. Rate of Onset to Reach Maximum Erection for Successful Quitters as a Function of Time. Bars represent mean slope values to reach maximum erectile response. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

More detailed examination of the data revealed that participants exhibited greater within-session erectile response ($t(20) = 2.73$, $p = .01$, $d = .60$) (16 of 21 men), greater maximum tumescence ($t(20) = 3.03$, $p = .01$, $d = .66$) (17 of 21 men), lower latency to reach maximum tumescence ($t(20) = 2.65$, $p = .02$, $d = .58$) (16 of 21 men), and faster erectile onset ($t(20) = 2.98$, $p = .01$, $d = .65$) (20 of 21 men), at mid-treatment compared to baseline. This corresponded to a 43%, 4%, and 106% increase in erectile response, maximum tumescence, and rate of onset, respectively, and a 30% reduction in time to reach maximum erection. There were no differences between baseline and mid-treatment

with respect to percent change in penile tumescence ($t(20) = 1.35$, $p = .19$, $d = .29$), or percent change in maximum tumescence ($t(20) = 1.81$, $p = .09$, $d = .38$).

All six indices were also improved at follow-up compared to baseline (raw change in erectile tumescence ($t(20) = 2.40$, $p = .03$, $d = .52$) (16 of 21 men); percent change in erectile tumescence ($t(20) = 2.27$, $p = .03$, $d = .45$) (16 of 21 men), raw change in maximum tumescence ($t(20) = 2.67$, $p = .02$, $d = .58$) (15 of 21 men); percent change in maximum tumescence ($t(20) = 3.69$, $p = .001$, $d = .74$) (15 of 21 men); latency to reach maximum tumescence ($t(20) = 2.58$, $p = .02$, $d = .56$) (16 of 21 men); and erectile onset ($t(20) = 2.68$, $p = .02$, $d = .58$) (20 of 21 men)). Participants showed a 44%, 40%, 5%, 48%, and 174% increase in raw change in erectile response, percent change in erectile tumescence, raw change in maximum tumescence, percent change in maximum tumescence, and rate of onset, respectively. Participants showed a 31% reduction in latency to reach maximum erection.

There was no difference between mid-treatment and follow-up with respect to any of the physiological sexual arousal variables (raw change in erectile tumescence ($t(20) = .07$, $p = .94$, $d = .02$); percent change in erectile tumescence ($t(20) = .07$, $p = .95$, $d = .01$); maximum tumescence ($t(20) = .17$, $p = .87$, $d = .04$); percent change in maximum tumescence ($t(20) = 1.07$, $p = .30$, $d = .23$); latency to reach maximum tumescence ($t(20) = .12$, $p = .90$, $d = .03$); and erectile onset ($t(20) = 1.60$, $p = .13$, $d = .35$)).

5.3.2 Analyses of continuous self-reported sexual arousal

Data from two participants were not interpretable because of software malfunction, and therefore analyses of subjective sexual arousal were conducted on the

remaining subsample with valid assessments (n = 19). Contrary to my hypotheses, one-way repeated measures ANOVAs revealed no significant across-session differences for within-session percent change ($F(2,36) = .01$, $p = .99$, $\eta^2 < .01$) (see Figure 9), latency to reach maximum arousal ($F(2,36) = .28$, $p = .76$, $\eta^2 = .02$) (see Figure 10), or rate of onset to maximum arousal ($F(2,36) = 1.67$, $p = .21$, $\eta^2 = .09$) (see Figure 11). This indicated that there was no effect of smoking cessation on self-reported sexual arousal.

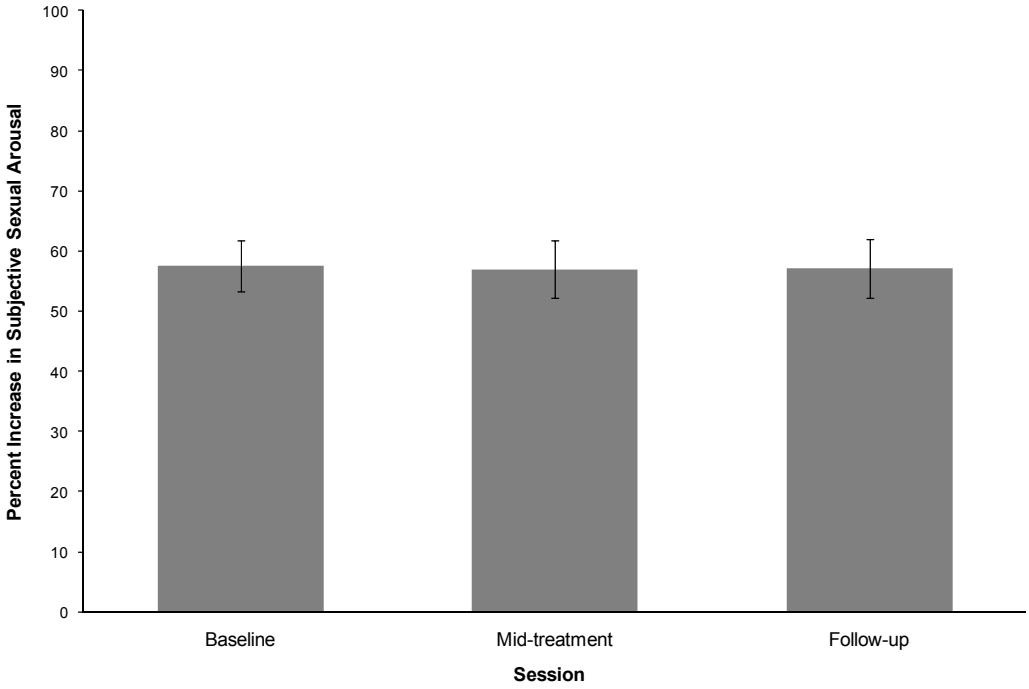

Figure 11. Percent Increase in Continuous Self-Reported Sexual Arousal for Successful Quitters as a Function of Time.
Bars represent mean percent increases in subjective sexual arousal (the difference between mean arousal scores during the erotic and neutral film stimuli divided by the mean of the neutral stimulus, and then multiplied by 100). Error bars represent standard errors of the means. Means were not significantly different from one another ($p > .05$).

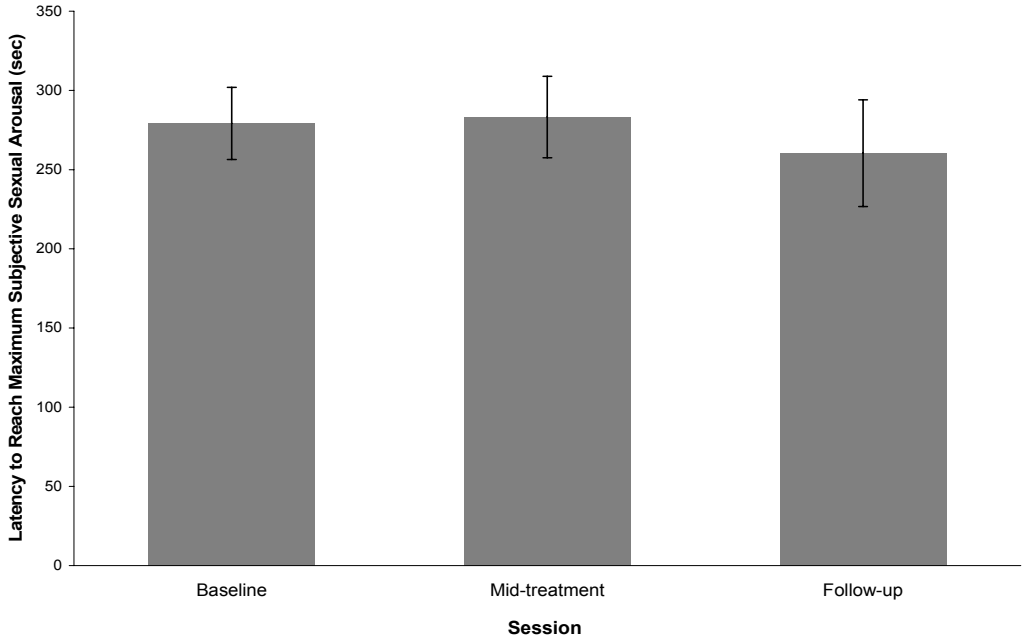

Figure 12. Time to Reach Maximum Self-Reported Sexual Arousal for Successful Quitters as a Function of Time.
Bars represent mean latencies to reach maximum subjective sexual arousal responses. Error bars represent standard errors of the means. Means were not significantly different from one another ($p > .05$).

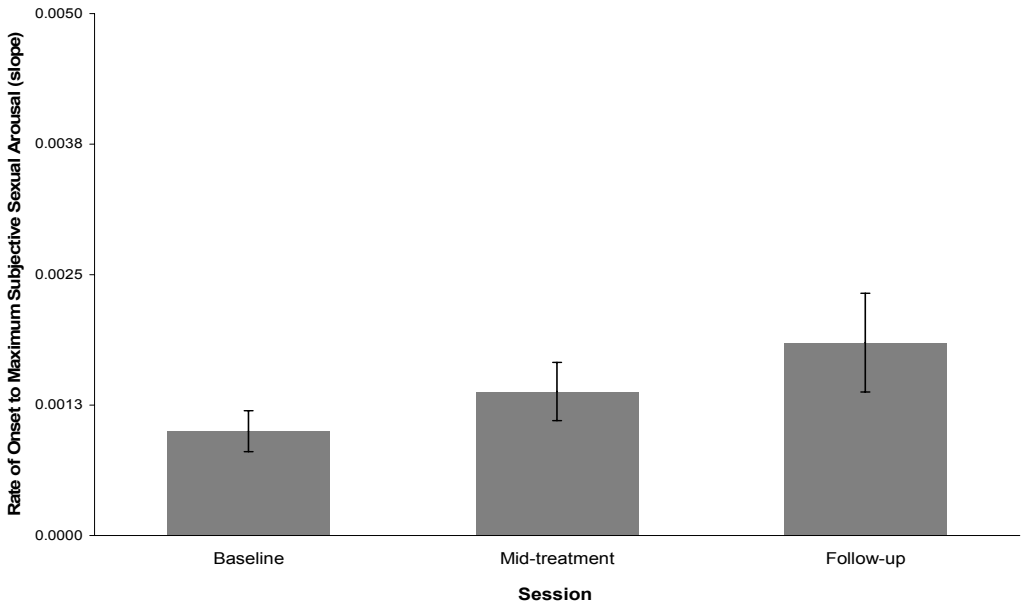

Figure 13. Rate of Onset to Reach Maximum Self-Reported Sexual Arousal for Successful Quitters as a Function of Time.
Bars represent mean slope values to reach maximum subjective sexual arousal responses. Error bars represent standard errors of the means. Means were not significantly different from one another ($p > .05$).

5.3.3 Analyses of the relationship between physiological and subjective sexual arousal responses

Analyses of men with valid physiological and subjective sexual arousal assessments for all sessions (n = 19), revealed that erectile responses and self-reported sexual arousal responses were significantly associated with one another at baseline ($r(17) = .67$, $p < .01$, $R^2 = .45$), but not at mid-treatment ($r(17) = .35$, $p = .15$, $R^2 = .12$) or at follow-up ($r(17) = .21$, $p = .40$, $R^2 = .04$). This was likely due to the fact that men did not show a differential change across time with respect to continuous subjective sexual arousal responses as they did with physiological genital arousal responses.

5.3.4 Analyses of self-reported sexual functioning

Participants demonstrated a significant main effect of time for erectile function ($F(2,40) = 4.69$, $p = .02$, $\eta^2 = .19$), intercourse satisfaction ($F(2,38) = 6.74$, $p < .01$, $\eta^2 = .26$), and overall sexual functioning ($F(2,40) = 6.23$, $p < .01$, $\eta^2 = .24$). Paired samples contrasts indicated that these measures significantly increased from baseline to follow-up (erectile function ($t(20) = 2.90$, $p < .01$, $d = .63$) (18 of 21 men); intercourse satisfaction ($t(20) = 2.01$, $p = .05$, $d = .44$) (16 of 21 men); overall sexual functioning ($t(20) = 3.13$, $p < .01$, $d = .68$) (14 of 21 men)), as well as from mid-treatment to follow-up (erectile function ($t(20) = 2.05$, $p < .05$, $d = .45$) (17 of 21 men); intercourse satisfaction ($t(20) = 2.17$, $p = .04$, $d = .47$) (19 of 21 men); overall sexual functioning ($t(20) = 2.44$, $p = .02$, $d = .53$) (16 of 21 men)). These variables did not differ from baseline to mid-treatment.

The other sexual function domains increased across sessions; however these differences did not reach statistical significance (orgasmic function ($F(2,40) = 1.99$, $p =$

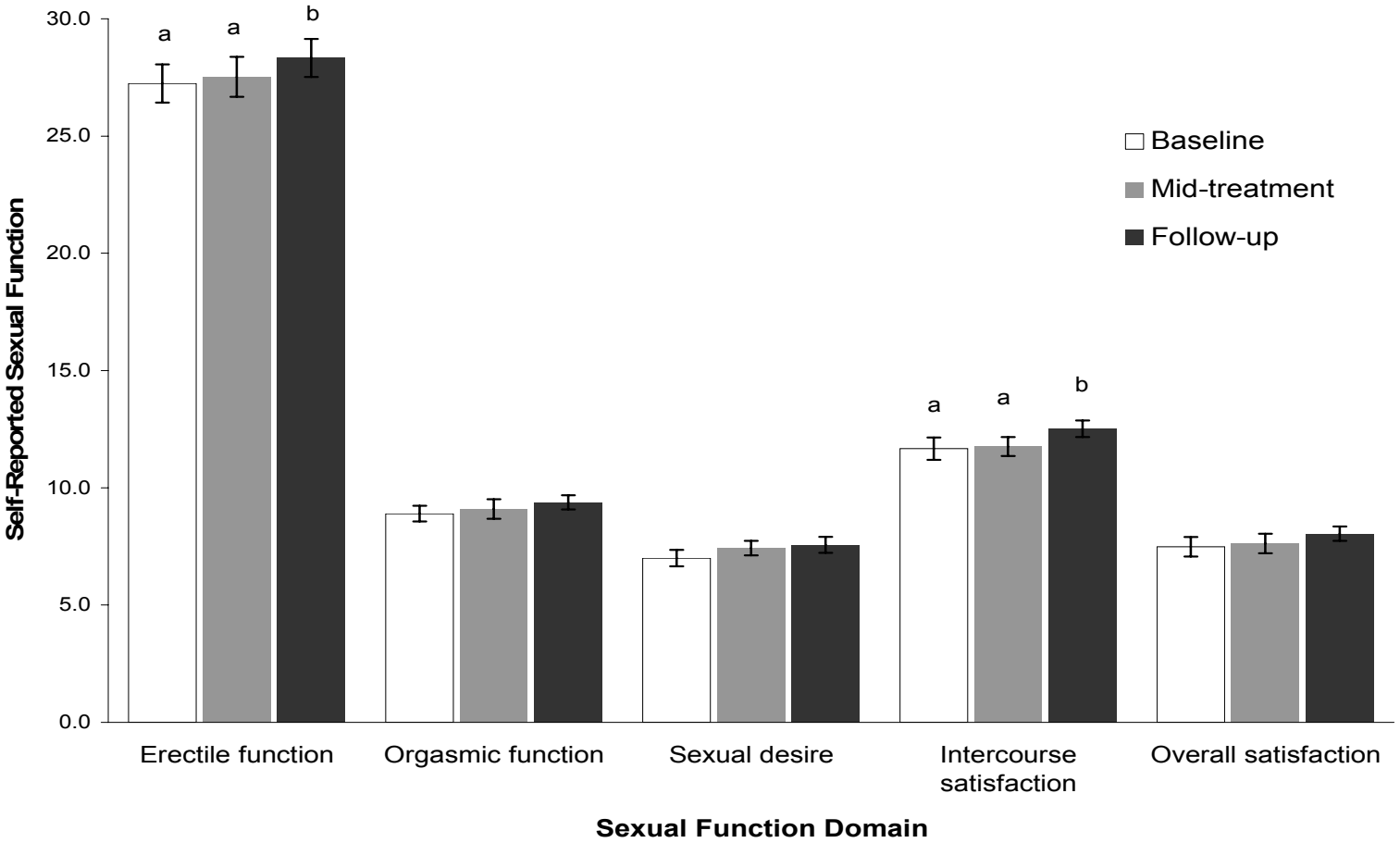

Figure 14. Changes in Sexual Function for Successful Quitters as a Function of Time.
Bars represent mean scores of sexual function domains of the IIEF. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$) within each IIEF domain. Bars without any superscripts were not statistically different from one another within each domain.

.16, $\eta^2 = .09$): sexual desire ($F(2,40) = 1.94$, $p = .16$, $\eta^2 = .09$); overall satisfaction ($F(2,40) = 1.42$, $p = .25$, $\eta^2 = .07$)). Mean IIEF sexual function domain scores for each session are presented in Figure 12.

With respect to changes in ED status as a function of smoking cessation, 24% (5 of 21) met criteria for ED at baseline, and 19% (4 of 21) and 5% (1 of 21) met criteria for ED at mid-treatment and follow-up, respectively. This corresponded to a statistically significant decrease in ED from both baseline to follow-up ($\chi^2(1) = 4.20$, $p < .05$; $\varphi = .45$) and from mid-treatment to follow-up ($\chi^2(1) = 4.46$, $p < .05$; $\varphi = .46$). There were no statistically significant changes from baseline to mid-treatment ($\chi^2(1) = .26$, $p = .68$; $\varphi = .11$).

5.3.5 Analyses of cardiovascular measures

Although participants showed improvements in cardiovascular measures, one-way repeated measures ANOVAs revealed no statistically significant across-session differences in systolic ($F(2,42) = 2.20$, $p = .13$, $\eta^2 = .10$) or diastolic ($F(2,42) = .88$, $p = .42$, $\eta^2 = .04$) blood pressures. With respect to analyses of heart rate, there was an overall main effect of time ($F(2,36) = 3.77$, $p = .05$, $\eta^2 = .17$), but no main effect of session ($F(2,36) = 2.12$, $p = .14$, $\eta^2 = .11$), and no significant time × session interaction ($F(4,36) = .41$, $p = .72$, $\eta^2 = .02$). This indicated that irrespective of smoking cessation, heart rates demonstrated significant within-session changes. More detailed analyses revealed higher heart rates during the erotic film compared to during the neutral film ($p = .001$, $d = .93$).

Heart rates assessed before film onset did not differ significantly from mean heart rates during the neutral film ($p = .10$, $d = .41$) or erotic film ($p = .67$, $d = .09$) presentations.

Participants showed differences in BMI across the three experimental sessions ($F(2,42) = 13.28$, $p < .001$, $\eta^2 = .39$). Specifically, men demonstrated significantly higher BMI at follow-up compared to both mid-treatment ($t(21) = 4.12$, $p < .001$, $d = .88$) and baseline ($t(21) = 4.02$, $p = .001$, $d = .86$), but did not show differences between baseline and mid-treatment ($t(21) = 1.93$, $p = .07$, $d = .41$). This indicated that men gained weight as a result of nicotine discontinuation (see Figure 13), which is a well-established phenomenon (Klesges, et al., 1997; Williamson, et al., 1991).

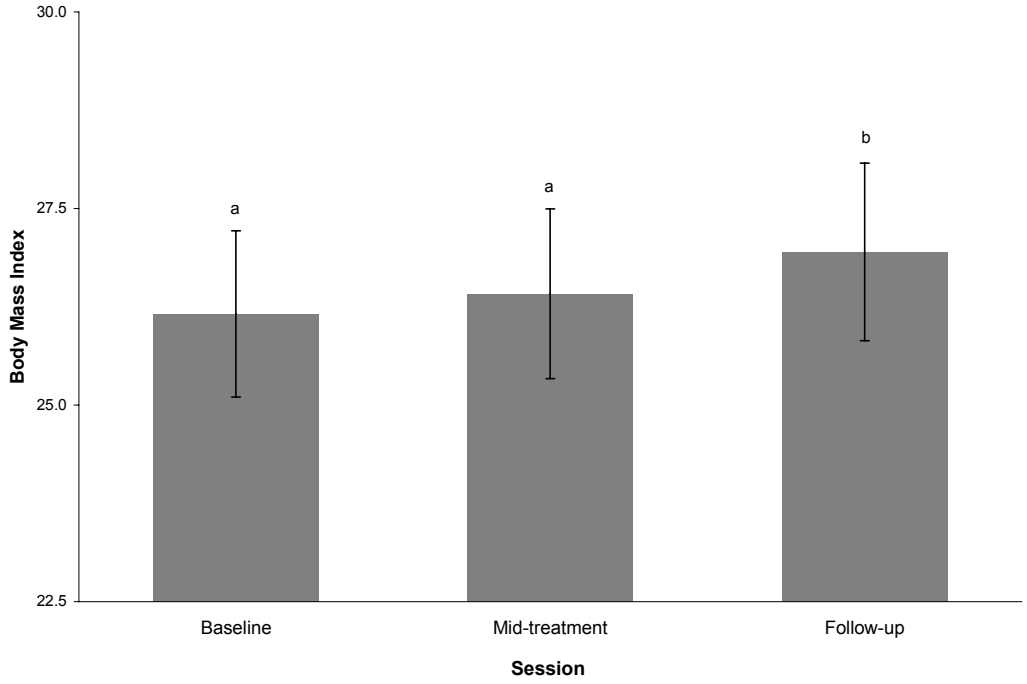

Figure 15. Changes in Body Mass Index for Successful Quitters as a Function of Time. Bars represent mean values. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another ($p < .05$).

5.3.6 Analyses using the last observation carried forward technique

Results of physiological sexual arousal analyses ($n = 47$) were similar to those using list-wise deletion (see Table 5 for overall summary of results; see Table 6 for across-session comparisons in terms of effect sizes for physiological sexual arousal by missing data approach). Specifically, there was a significant main effect of time for the six physiological sexual arousal variables (erectile tumescence raw change ($F(2,90) = 4.85$, $p = .02$, $\eta^2 = .10$); erectile tumescence percent change ($F(2,90) = 4.63$, $p = .01$, $\eta^2 = .10$); raw change in maximum erectile response ($F(2,90) = 7.84$, $p = .001$, $\eta^2 = .15$); percent change in maximum erectile response ($F(2,90) = 3.21$, $p = .05$, $\eta^2 = .08$); latency to reach maximum arousal ($F(2,90) = 4.77$, $p = .02$, $\eta^2 = .09$); rate of onset to maximum erection ($F(2,90) = 6.76$, $p < .01$, $\eta^2 = .13$).

Paired comparisons indicated greater within-session changes for all six physiological indices at mid-treatment compared to baseline: greater erectile tumescence raw values ($p = .03$, $d = .32$) (38 of 47 men), greater percent changes in erectile tumescence ($p = .04$, $d = .30$) (38 of 47 men), greater maximum tumescence ($p < .01$, $d = .42$) (40 of 47 men), greater percent increases in maximum tumescence ($p = .02$, $d = .34$) (40 of 47 men), lower latency to reach maximum tumescence ($p = .03$, $d = .34$) (39 of 47 men), and faster erectile onset ($p = .01$, $d = .38$) (44 of 47 men). This corresponded to a 21%, 22%, 3%, 20%, and 37% increase in erectile response, percent change in erectile tumescence, raw change in maximum tumescence, percent change in maximum tumescence, and rate of onset, respectively. Participants showed a 16% reduction in latency to reach maximum erection.

These indices were also improved at follow-up compared to baseline (raw change in erectile tumescence ($p = .02$, $d = .36$) (39 of 47 men); percent change in erectile tumescence ($p = .02$, $d = .35$) (39 of 47 men); maximum tumescence ($p < .01$, $d = .47$) (39 of 47 men); percent change in maximum tumescence ($p < .01$, $d = .46$) (39 of 47 men); latency to maximum tumescence ($p = .02$, $d = .34$) (38 of 47 men); erectile onset ($p < .01$, $d = .41$) (43 of 47 men)). Participants showed a 26%, 27%, 4%, 30%, and 56% increase in erectile response, percent increase in erectile tumescence, maximum tumescence, percent change in maximum tumescence, and rate of onset, respectively. Participants showed a 17% reduction in time to reach maximum erection.

There were no differences between mid-treatment and follow-up with respect to raw change in erectile tumescence ($p = .45$, $d = .11$), percent change in erectile tumescence ($p = .45$, $d = .11$), raw change in maximum tumescence ($p = .25$, $d = .17$), percent change in maximum tumescence ($p = .09$, $d = .25$), and latency to maximum tumescence ($p = .80$, $d = .04$)). Erectile onset was significantly improved at follow-up compared to mid-treatment ($p = .05$, $d = .29$).

Similar to list-wise deletion, there were no across-session differences in self-reported sexual arousal variables (percent change in sexual arousal ($F(2,90) = .03$, $p = .97$, $\eta^2 < .01$); latency to reach maximum arousal ($F(2,90) = .21$, $p = .81$, $\eta^2 = .01$); rate of onset to maximum arousal ($F(2,90) = 1.02$, $p = .35$, $\eta^2 = .02$) (see Table 5 and Table 7).

Participants again demonstrated differences in erectile function ($F(2,90) = 7.61$, $p = .001$, $\eta^2 = .15$), intercourse satisfaction ($F(2,90) = 5.37$, $p < .01$, $\eta^2 = .20$), and overall

	List-wise deletion (n = 19-21)			Last observation carried forward (n = 47)			Multiple imputation (n = 42)		
	Mid-treatment vs. baseline	Follow-up vs. baseline	Follow-up vs. mid-treatment	Mid-treatment vs. baseline	Follow-up vs. baseline	Follow-up vs. mid-treatment	Mid-treatment vs. baseline	Follow-up vs. baseline	Follow-up vs. mid-treatment
Physiological sexual arousal variables									
Magnitude of change in penile tumescence (mm)	MT > B**	FU > B*	ns	MT > B*	FU > B*	ns	MT > B**	FU > B**	ns
Percent change in penile tumescence	ns	FU > B*	ns	MT > B*	FU > B*	ns	MT > B*	FU > B**	ns
Maximum arousal (mm)	MT > B**	FU > B*	ns	MT > B**	FU > B**	ns	MT > B***	FU > B***	ns
Percent change in maximum arousal	ns	FU > B***	ns	MT > B*	FU > B**	ns	MT > B**	FU > B***	FU > MT*
Latency to reach maximum arousal (sec)	MT < B*	FU < B*	ns	MT < B*	FU < B*	ns	MT < B*	MT < B**	ns
Rate of onset to maximum erection (slope)	MT > B**	FU > B*	ns	MT > B**	FU > B**	FU > MT*	MT > B*	FU > B***	FU > MT***
Self-reported sexual arousal variables									
Percent change in arousal	ns	ns	ns	ns	ns	ns	ns	ns	ns
Latency to reach maximum arousal (sec)	ns	ns	ns	ns	ns	ns	ns	ns	ns
Rate of onset to maximum arousal (slope)	ns	ns	ns	ns	ns	ns	ns	ns	ns
Self-reported sexual functioning*									
Mean erectile function score	ns	FU > B**	FU > MT*	ns	FU > B***	FU > MT*	ns	FU > B***	FU > MT**
Mean orgasmic function score	ns	ns	ns	ns	ns	ns	ns	FU > B*	ns
Mean sexual desire score	ns	ns	ns	ns	FU > B*	ns	ns	ns	ns
Mean intercourse satisfaction score	ns	FU > B*	FU > MT*	ns	FU > B*	FU > MT**	ns	ns	ns
Mean overall satisfaction score	ns	ns	ns	ns	ns	ns	ns	ns	ns
Mean overall sexual functioning (total score)	ns	FU > B**	FU > MT*	ns	FU > B**	FU > MT**	ns	FU > B***	FU > MT**
Proportion meeting criteria for ED†	ns	FU < B*	FU < MT*	ns	FU < B**	FU < MT**	ns	FU < B**	FU < MT**

Table 5. Overall Results of Across-Session Comparisons within each Primary Outcome Variable by Missing Data Approach for Successful Quitters.
Abbreviations: B = baseline; ED = erectile dysfunction; FU = follow-up; MT = mid-treatment; ns = not statistically significant.
Note: *p < .05, **p < .01, ***p < .001
*As per the International Index of Erectile Function (IIEF).

sexual functioning ($F(2,90) = 7.73$, $p = .001$, $\eta^2 = .15$) (see Table 5 and Table 8).

Specifically, paired samples contrasts indicated significant increases from baseline to follow-up for erectile function ($p = .001$, $d = .50$) (43 of 47 men), intercourse satisfaction ($p = .04$, $d = .31$) (37 of 47 men), and overall sexual functioning ($p < .01$, $d = .49$) (37 of 47 men). Additionally, men showed increases from mid-treatment to follow-up for erectile function ($p = .02$, $d = .36$) (43 of 47 men), intercourse satisfaction ($p < .01$, $d = .40$) (45 of 47 men), and overall sexual functioning ($p < .01$, $d = .41$) (42 of 47 men). There were no statistically significant differences from baseline to mid-treatment (all ps > .05). Different from the list-wise technique, sexual desire became a significant sexual function domain using LOCF ($F(2,90) = 3.83$, $p = .03$, $\eta^2 = .08$), with men showing significantly higher sexual desire at follow-up compared to baseline ($p = .02$, $d = .35$), but not from baseline to mid-treatment ($p = .21$, $d = .19$), or from mid-treatment to follow-up ($p = .16$, $d = .21$). Orgasmic function ($F(2,90) = 2.66$, $p = .10$, $\eta^2 = .06$) and overall sexual satisfaction ($F(2,90) = .80$, $p = .44$, $\eta^2 = .02$) scores did not show statistically significant across-session differences.

With respect to changes in ED status as a function of smoking cessation, 28% (13 of 47) met criteria for ED at baseline, and 21% (10 of 47) and 11% (5 of 47) met criteria for ED at mid-treatment and follow-up, respectively. This corresponded to a statistically significant decrease in ED from both baseline to follow-up ($\chi^2(1) = 6.81$, $p = .01$; $\varphi = .38$) and from mid-treatment to follow-up ($\chi^2(1) = 7.76$, $p = .01$; $\varphi = .41$). There were no

statistically significant changes from baseline to mid-treatment ($\chi^2(1) = .75$, $p = .43$; $\varphi = .13$) (see Table 5 and Table 8).

5.3.7 Analyses using multiple imputation

Of the 2925 possible data points[†], 863 (29.5%) were missing and estimated with FIML procedures. The patterns of missing data in the current study were consistent with the assumption that the data are missing at random, as determined by Little's (1988) Missing Completely at Random Test ($\chi^2(304) = 72.84$, $p = .99$). Full information maximum likelihood was thus an appropriate estimator for the missing data.

Results of physiological sexual arousal analyses for men who were abstinent at follow-up ($n = 42$) were similar to analyses using both list-wise deletion and LOCF (see Tables 4 – 5). There was a significant main effect of time for raw changes in erectile tumescence ($F(2,80) = 3.98$, $p = .02$, $\eta^2 = .09$), maximum erectile response ($F(2,80) = 11.40$, $p < .001$, $\eta^2 = .22$), percent change in maximum erectile response ($F(2,80) = 4.14$, $p = .02$, $\eta^2 = .09$); time to reach maximum arousal ($F(2,80) = 4.39$, $p = .02$, $\eta^2 = .10$), and rate of onset to reach maximum erection ($F(2,80) = 4.69$, $p = .02$, $\eta^2 = .11$). There were no across-session differences in percent changes in erectile tumescence ($F(2,80) = 1.59$, $p = .21$, $\eta^2 = .04$).

Planned comparisons revealed that participants exhibited greater within-session erectile response ($p = .01$, $d = .40$) (29 of 42 men), greater maximum tumescence ($p = .001$, $d = .57$) (32 of 42 men), greater within-session percent increase in maximum

[†] (65 participants × 14 outcome variables × 3 assessments) + (65 participants × 3 smoking characteristic variables (end-point smoking status, total cigarette consumption throughout the study, total days of patch use).

tumescence ($p < .01$, $d = .45$) (32 of 42 men), smaller latency to reach maximum tumescence ($p = .05$, $d = .29$) (28 of 42 men), and faster erectile onset ($p = .02$, $d = .46$) (37 of 42 men) at mid-treatment compared to baseline. This corresponded to a 37%, 5%, 26%, and 49% increase in erectile response, maximum tumescence, percent increase in maximum tumescence, and rate of onset, respectively, and a 15% reduction in time to reach maximum erection.

These indices were also improved at follow-up compared to baseline (erectile tumescence ($p = .01$, $d = .39$) (30 of 42 men); maximum tumescence ($p = .001$, $d = .58$) (31 of 42 men); percent change in maximum tumescence ($p < .001$, $d = .75$) (31 of 42 men); latency to reach maximum tumescence ($p < .01$, $d = .45$) (30 of 42 men); and erectile onset ($p < .001$, $d = .62$) (38 of 42 men)). Participants showed a 32%, 5%, 41%, and 108% increase in erectile response, maximum tumescence, percent change in maximum erectile response, and rate of onset, respectively. Participants showed a 21% reduction in time to reach maximum erection.

There were no differences between mid-treatment and follow-up with respect to raw change in erectile tumescence, percent change in penile tumescence, maximum arousal, and latency to maximum arousal (all ps $> .05$). Both erectile onset ($p = .001$, $d = .67$) and percent change in maximum arousal ($p = .02$, $d = .40$) were significantly greater at follow-up compared to mid-treatment.

Similar to both list-wise deletion and LOCF, there were no across-session differences in percent change in self-reported sexual arousal ($F(2,80) = .42$, $p = .64$, $\eta^2 = .01$), latency to reach subjective maximum arousal ($F(2,80) = .25$, $p = .78$, $\eta^2 = .01$), or

	Baseline to mid-treatment				Baseline to follow-up				Mid-treatment to follow-up			
	Change	95% CI	*d*	*p*	Change	95% CI	*d*	*p*	Change	95% CI	*d*	*p*
List-wise deletion (*n* = 21)												
Magnitude of change in penile tumescence (mm)	2.86	.68, 5.04	.60	.01	2.93	.38, 5.48	.52	.03	.07	2.07 - 2.22	.02	.94
Percent change in penile tumescence	1.86	-1.01, 4.72	.29	.19	3.24	.89, 5.58	.45	.03	.07	-2.10, 2.24	.01	.95
Maximum arousal (mm)	5.13	1.60, 8.67	.66	.01	5.38	1.17, 9.59	.58	.02	.25	2.76 - 3.26	.04	.87
Percent change in maximum arousal	2.89	-.44, 6.23	.38	.09	6.29	2.89, 9.69	.74	.001	1.53	-1.44, 4.50	.23	.30
Latency to reach maximum arousal (sec)	-81.7	-146.16, -17.26	.58	.02	-84.2	-152.33, -16.03	.56	.02	-2.47	-43.95, -39.01	.03	.90
Rate of onset to maximum arousal*	5.67	1.70, 9.64	.65	.01	9.24	2.04, 16.45	.58	.02	3.57	1.08, 8.23	.35	.13
Last observation carried forward (*n* = 47)												
Magnitude of change in penile tumescence† (mm)	1.84	.17, 3.51	.32	.03	2.24	.43, 4.05	.36	.02	.40	-.66, 1.45	.11	.45
Percent change in penile tumescence	1.83	.06, 3.60	.30	.04	2.24	.35, 4.13	.35	.02	.41	-.66, 1.49	.11	.45
Maximum arousal† (mm)	3.67	1.08, 6.27	.42	<.01	4.78	1.77, 7.79	.47	<.01	1.11	-.80, 3.01	.17	.25
Percent change in maximum arousal	2.94	.43, 5.46	.34	.02	4.44	1.63, 7.25	.46	<.01	1.49	-.23, 3.22	.25	.09
Latency to reach maximum arousal† (sec)	-37.9	-70.87, -4.87	.34	.03	-40.1	-74.47, -5.69	.34	.02	-2.21	-19.95, 15.54	.04	.80
Rate of onset to maximum arousal*†	2.71	.62, 4.80	.38	.01	4.97	1.41, 8.54	.41	<.01	2.26	-.02, 4.54	.29	.05
Multiple imputation (*n* = 42)												
Magnitude of change in penile tumescence† (mm)	2.61	.58, 4.64	.40	.01	2.17	.46, 3.88	.39	.01	-.44	-2.01, 1.13	.02	.57
Percent change in penile tumescence	2.16	.41, 3.91	.39	.02	2.73	1.10, 4.37	.52	<.01	.57	-.65, 1.79	.15	.35
Maximum arousal† (mm)	6.12	2.78, 9.45	.57	.001	5.13	2.34, 7.92	.58	.001	.98	-3.05, 1.08	.15	.34
Percent change in maximum arousal	3.53	1.11, 5.95	.45	<.01	5.59	3.26, 7.92	.75	<.001	2.06	.37, 3.74	.40	.02
Latency to reach maximum arousal† (sec)	-40.4	-85.08, 4.23	.29	.05	-70.0	-108.56, 19.43	.45	<.01	-23.6	-52.90, 5.76	.25	.11
Rate of onset to maximum arousal*†	3.52	.62, 6.43	.46	.02	8.68	4.41, 12.95	.62	<.001	5.16	2.16, 8.15	.67	.001

Table 6. Across-Session Comparisons in Terms of Effect Sizes for each Physiological Sexual Arousal Measure by Missing Data Approach for Successful Quitters.

Abbreviations: CI = confidence interval; *d* = Cohen's d; *p* = two-tailed alpha value.

*Multiplied by 10^3.

†Based on adjusted cell means after controlling for age, pack years, and total cigarettes smoked throughout the study.

	Baseline to mid-treatment				Baseline to follow-up				Mid-treatment to follow-up			
	Change	95% CI	*d*	*p*	Change	95% CI	*d*	*p*	Change	95% CI	*d*	*p*
List-wise deletion (*n* = 19)*												
Percent change in arousal	-.59	-8.13, 6.94	.04	.87	-.43	-8.22, 7.36	.03	.91	.16	-10.21, 10.54	.01	.97
Latency to reach maximum arousal (sec)	4.05	-56.05, 64.16	.03	.89	-18.74	-85.60, 48.12	.14	.56	-22.79	-99.50, 53.91	.14	.54
Rate of onset to maximum arousal†	3.84	-.61, 8.29	.42	.09	8.53	-2.90, 19.95	.36	.13	4.68	-7.11, 16.49	.19	.42
Last observation carried forward (*n* = 46)‡												
Percent change in arousal¥	-.01	-3.24, 3.23	<.01	.99	.38	-3.09, 3.86	.03	.82	.39	-3.77, 4.55	.03	.85
Latency to reach maximum arousal¥ (sec)	6.73	-24.15, 37.62	.07	.66	-3.78	-38.85, 31.30	.03	.83	-10.51	-43.21, 22.19	.10	.52
Rate of onset to maximum arousal†¥	1.56	-1.40, 4.51	.16	.29	3.20	-2.15, 8.56	.18	.24	1.64	-3.22, 6.50	.10	.50
Multiple imputation (*n* = 42)												
Percent change in arousal¥	-2.76	-7.30, 1.78	.19	.23	.69	-3.34, 4.72	.05	.73	3.45	-2.36, 9.25	.19	.24
Latency to reach maximum arousal¥ (sec)	13.23	-30.92, 57.37	.09	.55	-22.06	-68.90, 24.78	.15	.35	-35.28	-82.45, 11.89	.23	.14
Rate of onset to maximum arousal†¥	-.97	-6.09, 4.15	.05	.70	7.22	.79, 15.66	.32	.08	6.19	.02, 13.65	.29	.07

Table 7. Across-Session Comparisons in Terms of Effect Sizes for each Subjective Sexual Arousal Measure by Missing Data Approach for Successful Quitters.

Abbreviations: CI = confidence interval; *d* = Cohen's d; *p* = two-tailed alpha value.

*Data missing for 2 participants.

†Multiplied by 10^4.

‡Data missing for 1 participant.

¥Based on adjusted cell means after controlling for age, pack years, and total cigarettes smoked throughout the study.

	Baseline to mid-treatment				Baseline to follow-up				Mid-treatment to follow-up			
	Change	95% CI	ES*	*p*	Change	95% CI	ES*	*p*	Change	95% CI	ES*	*p*
List-wise deletion (*n* = 21)												
Mean erectile function score	.29	-.42, .99	.18	.41	1.10	.31, 1.88	.63	<.01	.81	-.01, 1.63	.45	.05
Mean orgasmic function score	.19	-.26, .64	.19	.38	.48	-.06, 1.01	.41	.08	.29	-.24, .81	.25	.27
Mean sexual desire score	.43	-.18, 1.03	.32	.15	.57	-.14, 1.29	.36	.11	.14	-.42, .71	.12	.60
Mean intercourse satisfaction score	.10	-.62, .81	.06	.79	.86	-.03, 1.75	.44	.05	.76	.03, 1.50	.47	.04
Mean overall satisfaction score	.14	-.47, .76	.11	.63	.57	-.25, 1.39	.32	.16	.43	-.33, 1.18	.26	.25
Mean overall sexual functioning	1.14	-.84, 1.20	.26	.24	3.57	1.19, 5.95	.68	<.01	2.43	.35, 4.51	.53	.02
Number meeting criteria for ED†	-1	-6.07, 4.20	.11	.68	-4	-8.54, .67	.45	<.05	-3	-7.48, 1.46	.46	<.05
Last observation carried forward (*n* = 47)												
Mean erectile function score‡	.28	-.12, .67	.21	.17	.94	.38, 1.49	.50	.001	.63	.12, 1.14	.36	.02
Mean orgasmic function score‡	.13	-.20, .46	.11	.44	.39	-.01, .80	.29	.06	.26	-.04, .56	.26	.08
Mean sexual desire score‡	.21	-.12, .55	.19	.21	.48	.07, .88	.35	.02	.22	-.09, .52	.21	.16
Mean intercourse satisfaction score‡	<.01	-.45, .45	<.01	.99	.57	.03, 1.10	.31	.04	.50	.13, .87	.40	<.01
Mean overall satisfaction score‡	.04	-.26, .34	.04	.78	.22	-.20, .64	.15	.30	.17	-.19, .54	.14	.34
Mean overall sexual functioning‡	.67	-.53, 1.85	.16	.27	2.59	1.01, 4.17	.49	<.01	1.78	.51, 3.06	.41	<.01
Number meeting criteria for ED†	-3	-9.77, 5.21	.13	.43	-8	-15.20, .45	.38	.01	-5	-12.00, 2.12	.41	.01
Multiple imputation (*n* = 42)												
Mean erectile function score‡	.41	-.06, .88	.27	.09	1.25	.63, 1.87	.63	<.001	.84	.34, 1.34	.52	<.01
Mean orgasmic function score‡	.22	-.14, .57	.19	.23	.41	.01, .80	.32	.05	.19	-.09, .47	.21	.18
Mean sexual desire score‡	.39	-.09, .87	.25	.11	.58	.09, 1.08	.37	.02	.19	-.14, .53	.18	.25
Mean intercourse satisfaction score‡	.05	-.52, .61	.03	.86	.53	-.14, 1.21	.25	.12	.49	-.03, 1.00	.29	.06
Mean overall satisfaction score‡	.16	-.22, .55	.13	.40	.32	-.25, .90	.18	.26	.16	-.42, .74	.09	.57
Mean overall sexual functioning‡	1.44	.12, 2.99	.29	.07	3.16	1.43, 4.88	.57	.001	1.72	.62, 2.82	.49	<.01
Number meeting criteria for ED†	-1	-8.19, 6.25	.06	.72	-7	-13.26, -.82	.41	<.01	-6	-12.16, .01	.41	<.01

Table 8. Across-Session Comparisons in Terms of Effect Sizes for each Self-Reported Sexual Function Measure by Missing Data Approach for Successful Quitters.

Abbreviations: CI = confidence interval; ED = erectile dysfunction; ES = effect size.

*Effect sizes in Cohen's *d* for all variables, with the exception of number meeting criteria for ED, which is reported as Cramer's Phi.

†As per the IIEF erectile functioning cutoff score of 25.

‡Based on adjusted cell means after controlling for age, pack years, and total cigarettes smoked throughout the study.

rate of onset to maximum subjective sexual arousal ($F(2,80) = 1.81$, $p = .18$, $\eta^2 = .04$) (see Table 5 and Table 7).

Results of data analyses for sexual function using FIML for missing data are shown in Table 5 and Table 8. With multiple imputation techniques, participants again demonstrated differences in erectile function ($F(2,80) = 17.20$, $p < .001$, $\eta^2 = .30$), and overall sexual functioning ($F(2,80) = 5.17$, $p = .01$, $\eta^2 = .11$), with paired samples contrasts indicating significant increases from baseline to follow-up (erectile function ($p < .001$, $d = .63$) (37 of 42 men); overall sexual functioning ($p = .001$, $d = .57$) (30 of 42 men)), as well as from mid-treatment to follow-up (erectile function ($p < .01$, $d = .52$) (37 of 42 men); overall sexual functioning ($p < .01$, $d = 49$) (31 of 42 men)). There were no differences from baseline to mid-treatment with respect to these measures. With the FIML approach, orgasmic functioning became statistically significant ($F(2,80) = 6.01$, $p < .01$, $\eta^2 = .13$), with men demonstrating significantly higher orgasmic functioning at follow-up compared to baseline ($p = .05$, $d = 32$) (33 of 42 men). Sexual desire ($F(2,80) = 2.15$, $p = .13$, $\eta^2 = .05$), intercourse satisfaction ($F(2,80) = .01$, $p < .99$, $\eta^2 < .001$), and overall satisfaction ($F(2,80) = .63$, $p = .52$, $\eta^2 = .02$) scores did not show statistically significant across-session differences.

With respect to changes in ED status as a function of smoking cessation, 21% (9 of 42) met criteria for ED at baseline, and 19% (8 of 42) and 5% (2 of 42) met criteria for ED at mid-treatment and follow-up, respectively. This corresponded to a statistically significant decrease in ED from both baseline to follow-up ($\chi^2(1) = 6.93$, $p < .01$; $\varphi = .41$) and from mid-treatment to follow-up ($\chi^2(1) = 7.07$, $p < .01$; $\varphi = .41$). There were no

statistically significant changes from baseline to mid-treatment ($\chi^2(1) = .14$, $p = .72$; $\varphi = .06$) (see Table 5 and Table 8).

5.3.8 Post hoc analyses

Results of the linear regression analyses revealed no association between changes in positive affect (PA) and erectile tumescence ($r(22) = -2.72$, $p = .20$, adj $R^2 = .03$) or between negative affect (NA) and erectile tumescence ($r(22) = -.05$, $p = .82$, adj $R^2 = .04$) between baseline and follow-up. Similarly, there was no association between changes in PA or NA with respect to self-reported sexual arousal (PA: $r(22) = .28$, $p = .19$, adj $R^2 = .04$; NA: $r(22) = .06$, $p = .77$, adj $R^2 = .04$) or self-reported sexual functioning (PA: $r(22) = .24$, $p = .26$, adj $R^2 = .01$; NA: $r(22) = .07$, $p = .73$, adj $R^2 = .04$). Taken together, these results indicate that there was no statistically significant relationship between across-session changes in mood and sexual health indices. Analyses using LOCR and multiple imputation (FIML) produced similar results (see Table 9).

	Statistic			
	β	**Adjusted R^2**	***t***	***p***
List-wise deletion				
Physiological sexual arousal (*n* = 24)				
Positive affect	-.27	.03	-1.32	.20
Negative affect	-.05	.04	-.23	.82
Subjective sexual arousal* (*n* = 23)				
Positive affect	.28	.04	1.36	.19
Negative affect	.06	.04	.29	.77
Self-reported sexual function† (*n* = 24)				
Positive affect	.24	.01	1.15	.26
Negative affect	.07	.04	.34	.74
Last observation carried forward				
Physiological sexual arousal (*n* = 46)				
Positive affect	-.02	.02	-.15	.89
Negative affect	.13	.01	.87	.39
Subjective sexual arousal* (*n* = 45)				
Positive affect	.30	.07	1.76	.07
Negative affect	.08	.02	.55	.59
Self-reported sexual function*† (*n* = 45)				
Positive affect	.26	.05	1.78	.08
Negative affect	.07	.02	.48	.64
Multiple imputation				
Physiological sexual arousal (*n* = 42)				
Positive affect	-.18	.01	-1.16	.25
Negative affect	.03	.02	.18	.86
Subjective sexual arousal (*n* = 42)				
Positive affect	.24	.03	1.56	.13
Negative affect	.07	.02	.43	.67
Self-reported sexual function† (*n* = 42)				
Positive affect	-.01	<.01	-.07	.94
Negative affect	.17	<.01	1.06	.30

Table 9. Results of Association between Affect and each Primary Outcome Measure by Missing Data Approach for Successful Quitters.
*Data was missing for 1 participant.
†Measured with the International Index of Erectile Function.

5.4 Results of major study hypotheses for all participants (using intent-to-treat analyses)

5.4.1 Analyses of physiological sexual arousal

The results for the physiological sexual arousal outcome variables are summarized in Table 10, using 2 (group: successful quitter, relapser) × 3 (time: baseline, mid-treatment, follow-up) repeated measures ANCOVA. There was a significant group×time interaction effect for all six outcome measures: raw change in erectile tumescence ($F(4,124) = 4.44$, $p < .01$, $\eta^2 = .13$) (see Figure 16), percent change in penile tumescence ($F(4,124) = 8.93$, $p < .001$, $\eta^2 = .22$) (see Figure 17), raw change in maximum erectile response ($F(4,124) = 4.47$, $p < .01$, $\eta^2 = .13$) (see Figure 18), percent change in maximum erectile response ($F(4,124) = 5.17$, $p = .001$, $\eta^2 = .14$) (see Figure 19), latency to reach maximum arousal ($F(4,124) = 5.08$, $p = .001$, $\eta^2 = .14$) (see Figure 20), and rate of onset to maximum erection ($F(4,124) = 4.74$, $p = .001$, $\eta^2 = .13$) (see Figure 21).

Post-hoc tests of between-subjects contrasts revealed significantly greater percent increases in erectile tumescence at follow-up among successful quitters compared to those that relapsed ($p = .02$, $d = .31$). Successful quitters, compared to relapsers, also demonstrated a statistical trend toward greater within-session changes in penile tumescence ($p = .08$, $d = .22$) and greater within-session percent change in maximum erection ($p = .09$, $d = .21$) at the follow-up evaluation. There were no between-group differences at baseline or mid-treatment for these outcome measures (all ps > .05).

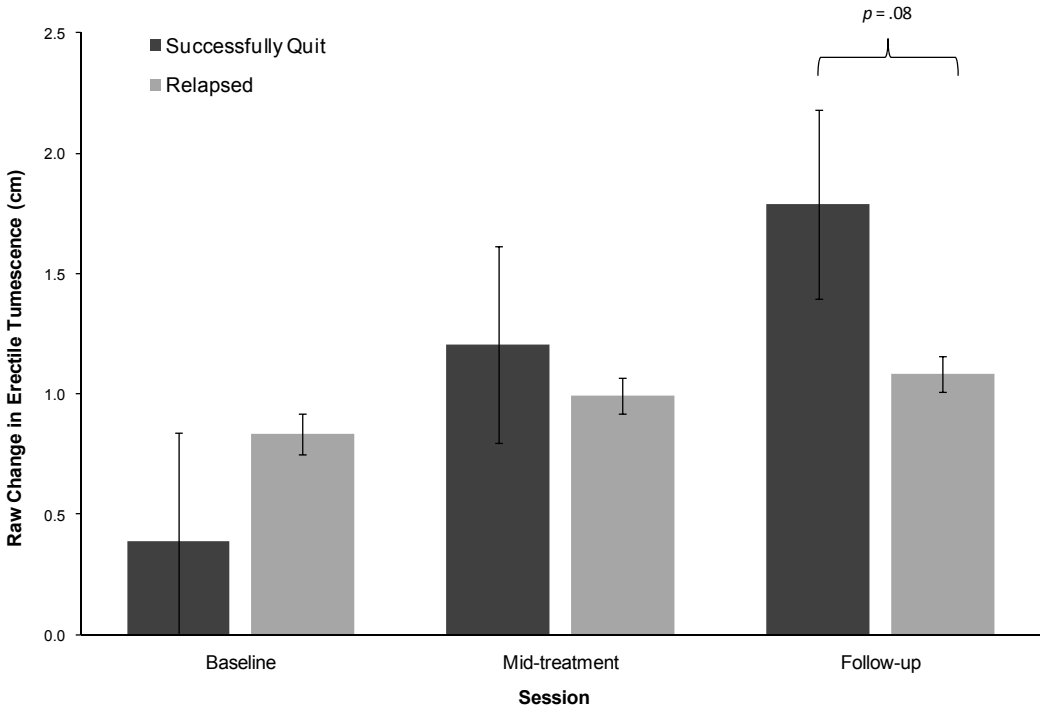

Figure 16. Raw Changes in Erectile Tumescence for all Participants as a Function of Time. Bars represent mean within-session erectile tumescence change scores (mean tumescence during erotic stimulus minus mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

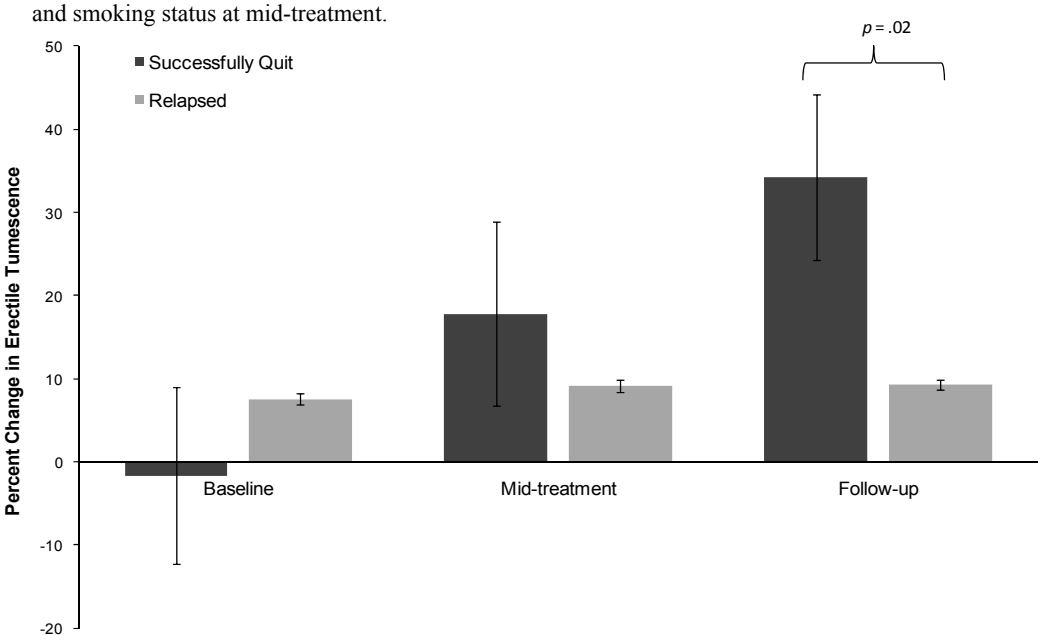

Figure 17. Percent Changes in Erectile Tumescence for all Participants as a Function of Time. Bars represent mean within-session percent changes in erectile tumescence (mean tumescence during erotic stimulus minus mean tumescence during neutral stimulus divided by mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

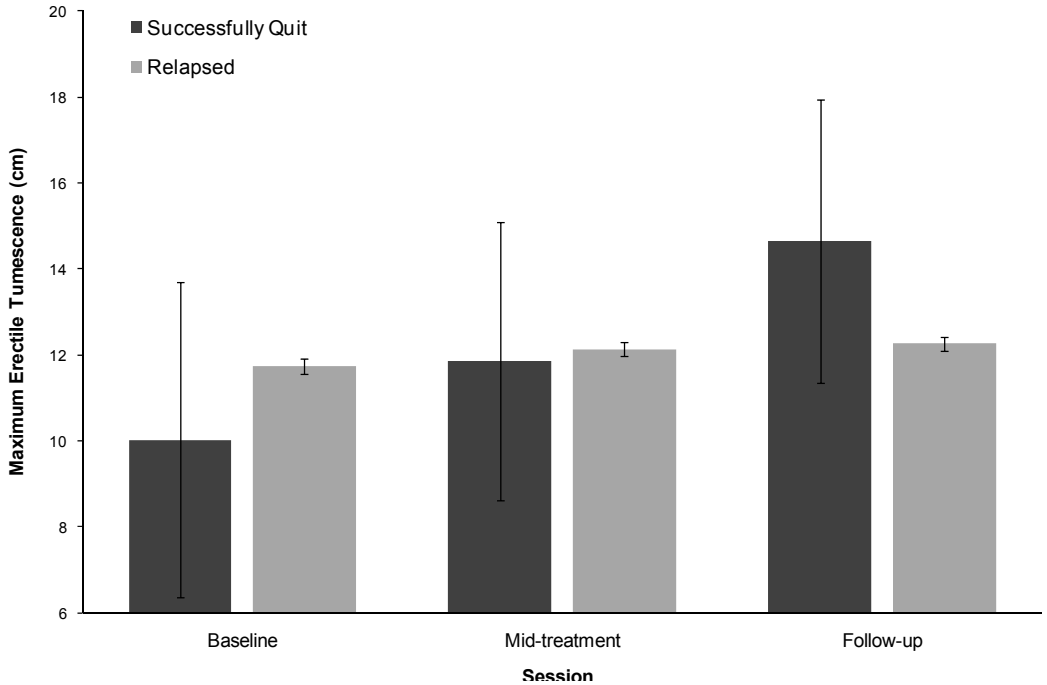

Figure 18. Raw Changes in Maximum Erectile Response for all Participants as a Function of Time. Bars represent mean maximum erectile tumescence scores. Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

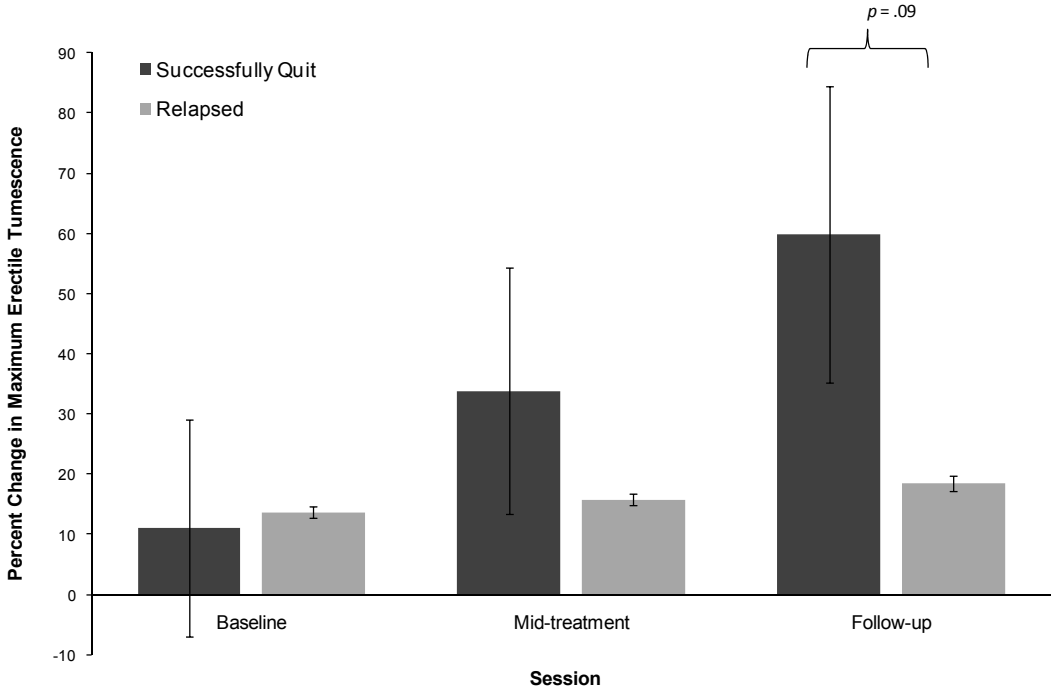

Figure 19. Percent Changes in Maximum Erectile Response for all Participants as a Function of Time. Bars represent mean within-session percent changes in maximum erectile tumescence scores (maximum tumescence during erotic stimulus minus mean tumescence during neutral stimulus divided by mean tumescence during neutral stimulus). Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

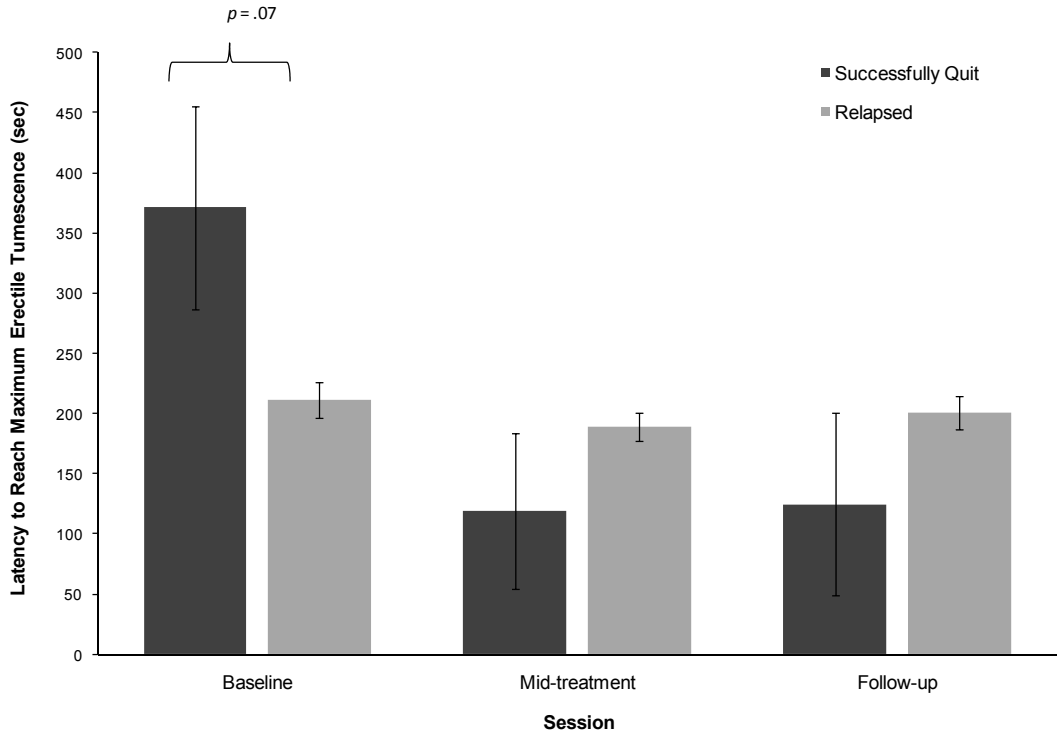

Figure 20. Latency to Reach Maximum Erection for all Participants as a Function of Time.
Bars represent mean latencies to reach maximum erectile response. Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

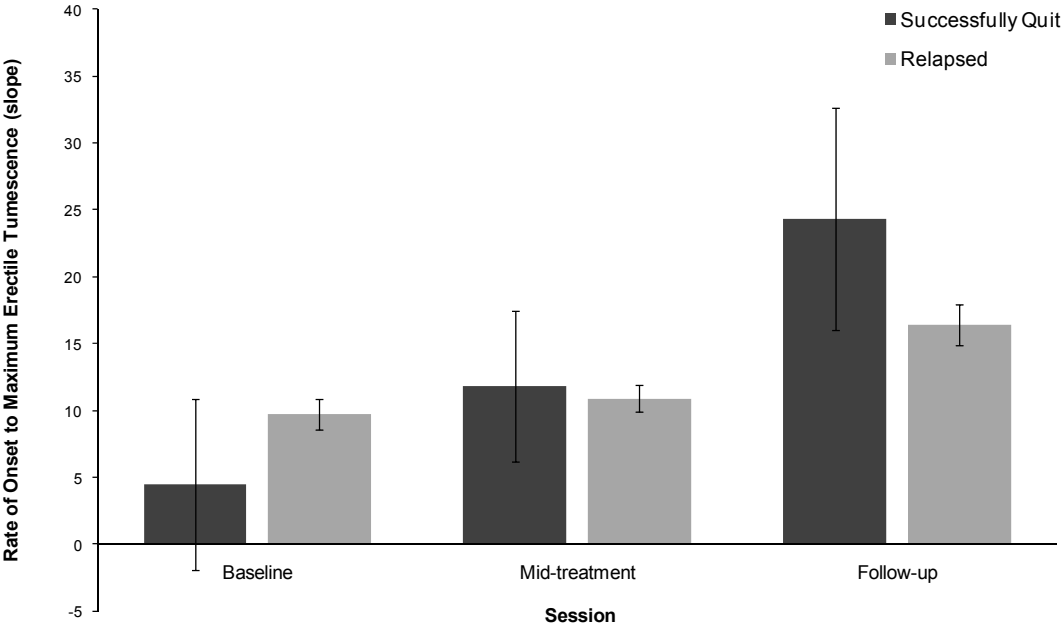

Figure 21. Rate of Onset to Reach Maximum Erection for all Participants as a Function of Time.
Bars represent mean slope values to reach maximum erectile response. Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

Outcome measure	Successful quitters (n = 20)			Unsuccessful quitters (n = 45)			
	Mean*	(SE)*	[95% CI]*	Mean*	(SE)*	[95% CI]*	*P* value†
Raw change in penile tumescence							
Baseline	.39	(.45)	[-.52, 1.29]	.83	(.08)	[.67, 1.00]	
Mid-treatment	1.21	(.41)	[.39, 2.02]	.99	(.08)	[.84, 1.14]	<.01
4-week follow-up	1.79	(.39)	[1.00, 2.57]	1.08	(.07)	[.94, 1.23]	
Percent change in penile							
Baseline	-1.70	(10.62)	[-22.92, 19.53]	7.56	(.69)	[6.17, 8.94]	
Mid-treatment	17.80	(11.01)	[-4.22, 39.81]	9.11	(.72)	[7.68, 10.55]	<.001
4-week follow-up	34.20	(9.95)	[14.31, 54.09]	9.29	(.65)	[7.99, 10.58]	
Maximum penile tumescence (cm)							
Baseline	10.02	(3.67)	[2.68, 17.37]	11.73	(.18)	[11.36, 12.09]	
Mid-treatment	11.85	(3.25)	[5.36, 18.35]	12.14	(.16)	[11.82, 12.45]	<.01
4-week follow-up	14.65	(3.30)	[8.05, 21.25]	12.26	(.16)	[11.94, 12.59]	
Percent change in maximum tumescence (cm)							
Baseline	11.01	(18.01)	[-24.98, 46.99]	13.69	(.89)	[11.92, 15.46]	
Mid-treatment	33.83	(20.55)	[-7.24, 74.90]	15.78	(1.01)	[13.76, 17.80]	.001
4-week follow-up	59.81	(24.58)	[10.67, 108.94]	18.43	(1.21)	[16.01, 20.85]	
Latency to reach maximum arousal (sec)							
Baseline	371	(84.1)	[202.8, 539.1]	211	(15.4)	[180.8, 242.3]	
Mid-treatment	119	(64.9)	[-11.1, 248.5]	190	(11.9)	[166.2, 213.7]	.001
4-week follow-up	125	(75.9)	[-26.8, 276.5]	201	(13.9)	[173.7, 229.1]	
Rate of onsent to maximum arousal (slope)‡							
Baseline	4.5	(6.41)	[-8.26, 17.37]	9.7	(1.17)	[7.38, 12.06]	
Mid-treatment	11.8	(5.64)	[.54, 23.12]	10.9	(1.03)	[8.81, 12.93]	.001
4-week follow-up	24.3	(8.32)	[7.61, 40.89]	16.4	(1.52)	[13.38, 19.46]	

Table 10. Summary of Results for Intent-to-Treat Analyses of Physiological Sexual Arousal.
Abbreviations: CI = confidence interval; SE = standard error.
*Adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.
†P value based on Greenhouse-Geisser adjustment for the interaction between group and time from analysis of variance (ANOVA) model covarying for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.
‡Original values multiplied by 10^3.

Additionally, there was a statistically significant improvement in successful quitters versus relapsers at both mid-treatment ($p < .01$, $d = .66$) and 4-week follow-up ($p < .01$, $d = .67$), compared with baseline, for latency to maximum arousal. There were no between-group differences in maximum tumescence; both groups displayed significant within-group improvements at follow-up compared to baseline (successful quitters: $p = .03$; $d = .52$; relapsers: $p = .01$, $d = .70$), however, participants that relapsed also demonstrated improvement at mid-treatment compared to baseline ($p < .001$, $d = .62$). Finally, with respect to erectile onset, both groups displayed significant within-group improvements at follow-up compared to baseline (successful quitters: $p = .04$; $d = .50$; relapsers: $p < .001$, $d = .54$); however, participants that relapsed, compared to those that quit successfully, also demonstrated improvement at follow-up compared to mid-treatment ($p < .001$, $d = .80$).

5.4.2 Analyses of continuous self-reported sexual arousal

Results for the subjective sexual arousal outcome variables are summarized in Table 11, using 2 (group: successful quitter, relapser) × 3 (time: baseline, mid-treatment, follow-up) repeated measures ANCOVA. Contrary to my hypotheses, there were no significant group×time interaction effects for within-session percent change ($F(4,124) = 1.47$, $p = .22$, $\eta^2 = .05$) (see Figure 22) or for latency to reach maximum arousal ($F(4,124) = 1.70$, $p = .15$, $\eta^2 = .05$) (see Figure 23).

There was, however, a statistically significant group×time interaction for rate of onset to maximum arousal ($F(4,124) = 4.64$, $p < .01$, $\eta^2 = .13$) (see Figure 24). Post-hoc tests of between-subjects contrasts revealed significantly greater rate of erectile onset at

follow-up among successful quitters compared to those that relapsed ($p < .001$, $d = .50$). Groups did not differ at baseline or mid-treatment for this measure (all ps > .05).

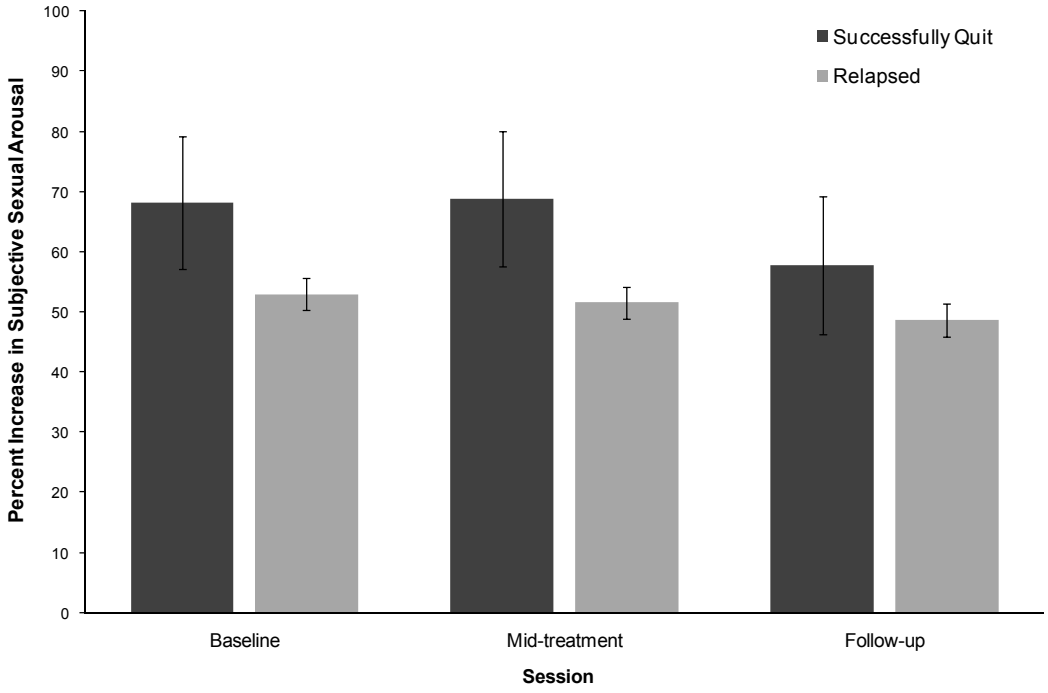

Figure 22. Percent Increase in Continuous Self-Reported Sexual Arousal for all Participants as a Function of Time.
Bars represent mean percent increases in subjective sexual arousal (the difference between mean arousal scores during the erotic and neutral film stimuli divided by the mean of the neutral stimulus, and then multiplied by 100). Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment. Means were not significantly different from one another ($p > .05$).

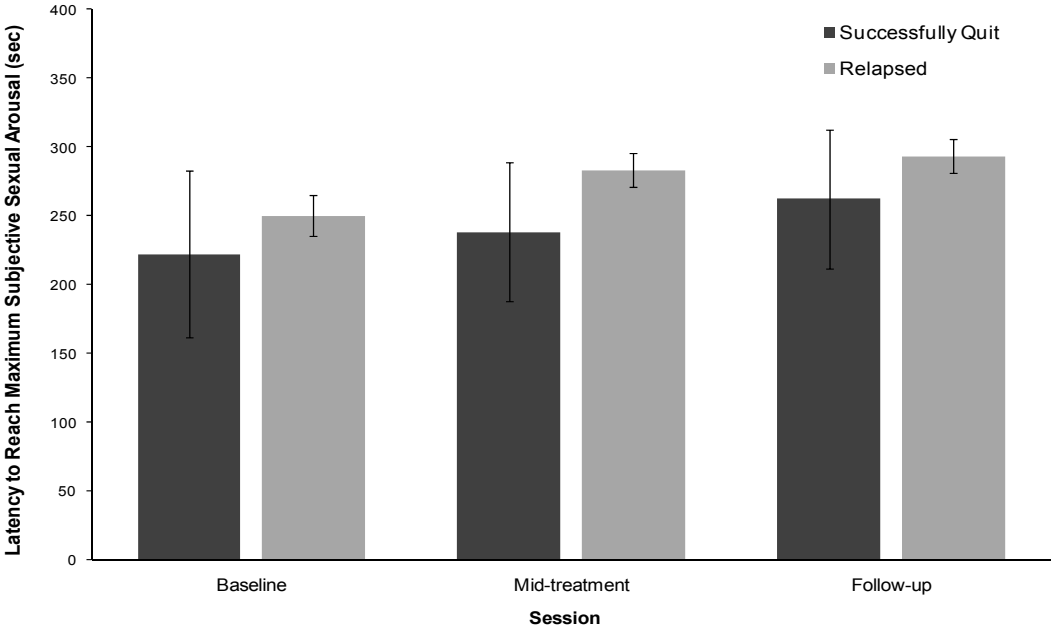

Figure 23. Latency to Reach Maximum Self-Reported Sexual Arousal for all Participants as a Function of Time.

Bars represent mean latencies to reach maximum subjective sexual arousal responses. Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment. Means were not significantly different from one another ($p > .05$).

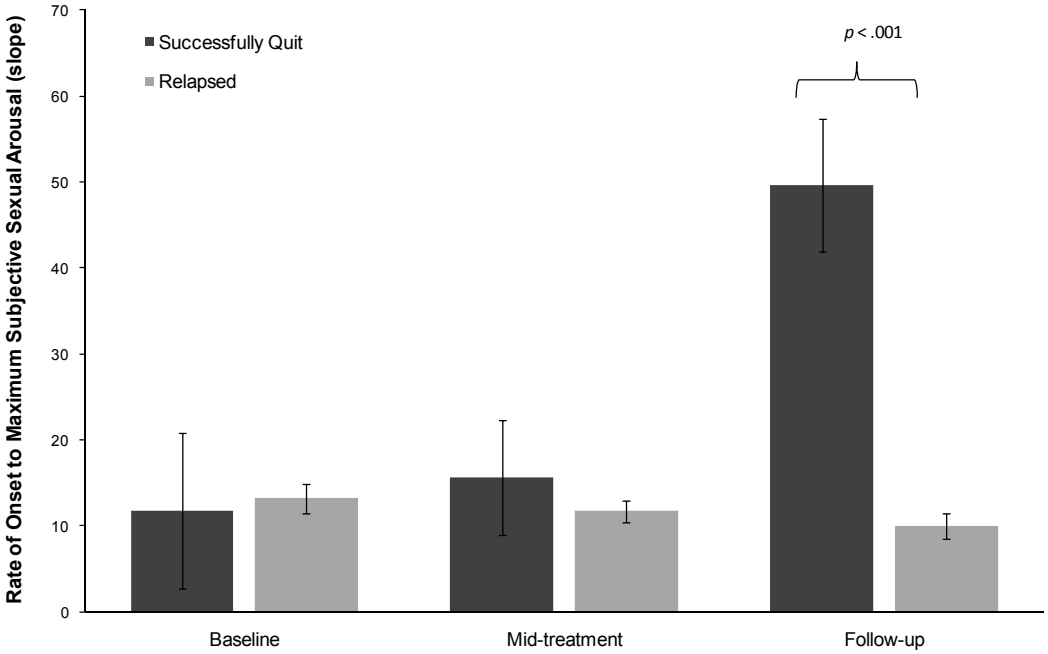

Figure 24. Rate of Onset to Reach Maximum Self-Reported Sexual Arousal for all Participants as a Function of Time.

Bars represent mean slope values to reach maximum subjective sexual arousal responses. Error bars represent standard errors of the means. Means have been adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, and smoking status at mid-treatment.

Outcome measure	Successful quitters (n = 20)			Unsuccessful quitters (n = 45)			
	Mean*	(SE)*	[95% CI]*	Mean*	(SE)*	[95% CI]*	*P* value†
Percent change in subjective sexual arousal							
Baseline	68.1	(11.01)	[45.99, 90.03]	52.9	(2.68)	[47.56, 58.29]	
Mid-treatment	68.7	(11.24)	[46.21, 91.14]	51.5	(2.74)	[45.99, 56.94]	.22
4-week follow-up	57.8	(11.46)	[34.86, 80.71]	48.6	(2.79)	[43.05, 54.21]	
Latency to maximum subjective sexual arousal (sec)							
Baseline	222	(60.6)	[100.5, 342.8]	250	(14.8)	[221.2, 280.3]	
Mid-treatment	238	(50.4)	[137.2, 338.7]	283	(12.3)	[258.1, 307.2]	.15
4-week follow-up	262	(50.4)	[161.3, 362.6]	293	(12.3)	[268.4, 317.4]	
Rate of onsent to maximum subjective sexual arousal (slope)‡							
Baseline	11.8	(9.04)	[-6.32, 29.85]	13.2	(1.74)	[9.68, 16.65]	
Mid-treatment	15.6	(6.73)	[2.14, 29.04]	11.7	(1.29)	[9.15, 14.33]	<.01
4-week follow-up	49.6	(7.69)	[34.26, 65.00]	10.0	(1.48)	[7.08, 13.02]	

Table 11. Summary of Results for Intent-to-Treat Analyses of Subjective Sexual Arousal.
Abbreviations: CI = confidence interval; SE = standard error.
*Adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.
†P value based on Greenhouse-Geisser adjustment for the interaction between group and time from analysis of variance (ANOVA) model covarying for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.
‡Original values multiplied by 10^4.

5.4.3 Analyses of the relationship between physiological and subjective sexual arousal responses

Analyses of the entire sample revealed that physiological erectile responses and self-reported sexual arousal responses were significantly associated with one another at baseline ($r(63) = .33$, $p < .01$, adj $R^2 = .10$) and mid-treatment ($r(63) = .43$, $p < .001$, adj $R^2 = .17$), but not at follow-up ($r(63) = .23$, $p = .07$, adj $R^2 = .04$). With respect to the two treatment groups, successful quitters demonstrated a significant association between physiological and self-reported genital responses at the baseline evaluation ($r(18) = .58$, $p < .01$, adj $R^2 = .30$), but not at the mid-treatment assessment ($r(18) = .30$, $p = .20$, adj $R^2 = .04$). Unsuccessful quitters displayed significant concordance between these two measures at both baseline ($r(43) = .31$, $p = .04$, adj $R^2 = .08$) and mid-treatment ($r(43) = .48$, $p < .001$, adj $R^2 = .21$). Neither of the two groups showed a significant relationship between physiological and subjective sexual arousal at follow-up (successful quitters: $r(18) = .17$, $p = .48$, adj $R^2 = .03$; unsuccessful quitters: $r(43) = .26$, $p = .08$, adj $R^2 = .05$). Lack of genital-subjective concordance was likely due to the fact that men did not show a robust pattern of differential change across time with respect to continuous subjective sexual arousal responses as they did with physiological genital arousal responses.

5.4.4 Analyses of self-reported sexual functioning

Results of the self-reported sexual function outcome variables are summarized in Table 12, using 2 (group: successful quitter, relapser) × 3 (time: baseline, mid-treatment, follow-up) repeated measures ANCOVA. Contrary to my hypotheses, there were no

statistically significant group×time interaction effects for any of the indices: erectile function ($F(4,124) = .51$, $p = .66$, $\eta^2 = .02$); orgasmic function ($F(4,124) = 1.28$, $p = .29$, $\eta^2 = .04$), sexual desire ($F(4,124) = 1.01$, $p = .36$, $\eta^2 = .03$), intercourse satisfaction ($F(4,124) = .55$, $p = .65$, $\eta^2 = .02$), overall satisfaction ($F(4,124) = .51$, $p = .73$, $\eta^2 = .02$), overall sexual function ($F(4,124) = .59$, $p = .67$, $\eta^2 = .02$). This indicated that quitting smoking had no effect on self-reported sexual functioning.

With respect to changes in ED status as a function of smoking cessation, 20% (4 of 20) of successful quitters met criteria for ED at baseline, and 20% (4 of 20) and 5% (1 of 19) met criteria for ED at mid-treatment and follow-up, respectively. Among, unsuccessful quitters, 33% (15 of 45) met criteria for ED at baseline, and 22% (10 of 45) and 13% (6 of 45) met criteria for ED at mid-treatment and follow-up, respectively (see Figure 25). This corresponded to a remission rate of 75% for successful quitters and 61% for unsuccessful quitters. There were no between-group differences in the rates of ED at any time point (baseline: $\chi^2(1) = 1.19$, $p = .28$; $\varphi = .14$; mid-treatment: $\chi^2(1) = .04$, $p = .84$; $\varphi = .03$; follow-up: $\chi^2(1) = .62$, $p = .43$; $\varphi = .10$. Similarly multivariate logistic regression analyses did not reveal any statistically significant association between quitting smoking and erectile dysfunction status at either mid-treatment (adjusted odds ratio (AOR) = 1.90; $p = .61$; CI = .16, 22.57) or 4-week follow-up (AOR = 145.5; $p = .11$; CI = .30, 70,179.45).

Outcome measure	Successful quitters ($n = 20$)			Unsuccessful quitters ($n = 45$)			*P* value†
	Mean*	(SE)*	[95% CI]*	Mean*	(SE)*	[95% CI]*	
Erectile function							
Baseline	29.0	(4.53)	[19.91, 38.04]	26.9	(.65)	[25.69, 28.28]	
Mid-treatment	30.6	(3.32)	[23.98, 37.24]	27.7	(.47)	[26.77, 28.66]	.66
4-week follow-up	30.4	(2.62)	[25.17, 35.65]	28.5	(.38)	[27.76, 29.26]	
Orgasmic function							
Baseline	10.3	(1.40)	[7.47, 13.04]	9.0	(.20)	[8.62, 9.42]	
Mid-treatment	10.2	(1.30)	[7.56, 12.75]	9.4	(.19)	[8.98, 9.72]	.29
4-week follow-up	9.2	(.99)	[7.21, 11.18]	9.6	(.14)	[9.36, 9.93]	
Sexual desire							
Baseline	5.9	(1.50)	[2.93, 8.93]	7.4	(.21)	[6.98, 7.84]	
Mid-treatment	7.7	(1.58)	[4.54, 10.84]	7.3	(.23)	[6.80, 7.70]	.36
4-week follow-up	7.7	(1.53)	[4.62, 10.75]	7.6	(.22)	[7.21, 8.09]	
Intercourse satisfaction							
Baseline	11.5	(2.58)	[6.37, 16.67]	11.8	(.37)	[11.10, 12.57]	
Mid-treatment	11.2	(1.90)	[7.43, 15.04]	11.9	(.27)	[11.34, 12.43]	.65
4-week follow-up	13.0	(1.93)	[11.94, 13.04]	12.4	(.28)	[11.94, 13.04]	
Overall sexual satisfaction							
Baseline	7.2	(1.18)	[4.85, 9.57]	7.8	(.24)	[7.28, 8.26]	
Mid-treatment	8.4	(1.17)	[6.04, 10.73]	7.5	(.24)	[6.99, 7.96]	.73
4-week follow-up	8.0	(1.01)	[5.98, 10.02]	8.0	(.21)	[7.59, 8.42]	
Overall sexual functioning							
Baseline	63.6	(6.25)	[51.12, 76.12]	62.9	(1.29)	[60.29, 65.43]	
Mid-treatment	66.9	(4.95)	[57.09, 76.87]	63.9	(1.02)	[61.83, 65.90]	.67
4-week follow-up	67.4	(4.41)	[58.56, 76.20]	66.4	(.91)	[64.59, 68.22]	

Table 12. Summary of Results for Intent-to-Treat Analyses of Self-Reported Sexual Function.
Abbreviations: CI = confidence interval; SE = standard error.
*Adjusted for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.
†P value based on Greenhouse-Geisser adjustment for the interaction between group and time from analysis of variance (ANOVA) model covarying for pack years, total cigarette consumption throughout enrollment, baseline erectile functioning, baseline drinking severity, and smoking status at mid-treatment assessment.

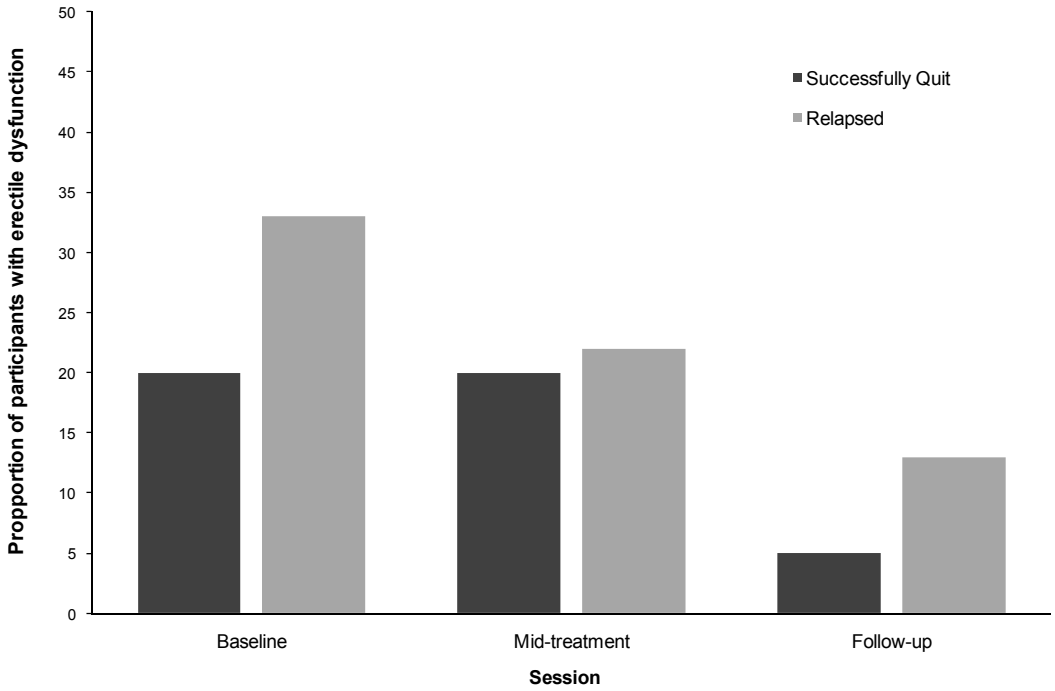

Figure 25. Proportion of Men Meeting Criteria for Erectile Dysfunction as a Function of Time. Bars represent within-group proportions.

5.4.5 Analyses of cardiovascular measures

Results for the cardiovascular measures are summarized in Table 13, using a series of 2 (group: successful quitter, relapser) × 3 (time: baseline, mid-treatment, follow-up) repeated measures ANCOVA, controlling for pack years, BMI, baseline activity level, baseline drinking severity, and smoking status at the mid-treatment evaluation. Although participants showed improvements in cardiovascular measures, the analyses revealed no statistically significant interaction effects for across-session changes in systolic ($F(4,124) = 2.04$, $p = .10$, $\eta^2 = .06$) or diastolic ($F(4,124) = .20$, $p = .90$, $\eta^2 = .01$) blood pressures. There was also no significant interaction effect resting heart rate ($F(4,124) = .15$, $p = .96$, $\eta^2 = .01$). Taken together, these data indicate that those who quit smoking did not show relative short-term improvements in cardiovascular measures compared to those individuals who relapsed.

With respect to across-session changes in BMI, there was a moderately statistically significant group×time interaction effect ($F(4,124) = 2.17$, $p = .07$, $\eta^2 = .07$) (see Figure 26 and Table 13). Post-hoc tests revealed that successful quitters, compared to those that relapsed, demonstrated a significant overall main effect of time ($F(2,61) = 6.67$, $p < .01$, $\eta^2 = .18$. Post hoc tests of within-subjects contrasts indicated that successful quitters displayed significantly higher BMI scores at mid-treatment compared to baseline ($p = .03$, $d = .83$), as well as at follow-up compared to baseline ($p = .001$, $d = .31$). There was a statistical trend toward higher BMI at follow-up compared to mid-treatment ($p = .08$, $d = .39$).

Taken together, these results in indicated that successful quitters, compared to men that relapsed, gained weight as a result of nicotine discontinuation, which is in line with established findings (Klesges, et al., 1997; Williamson, et al., 1991).

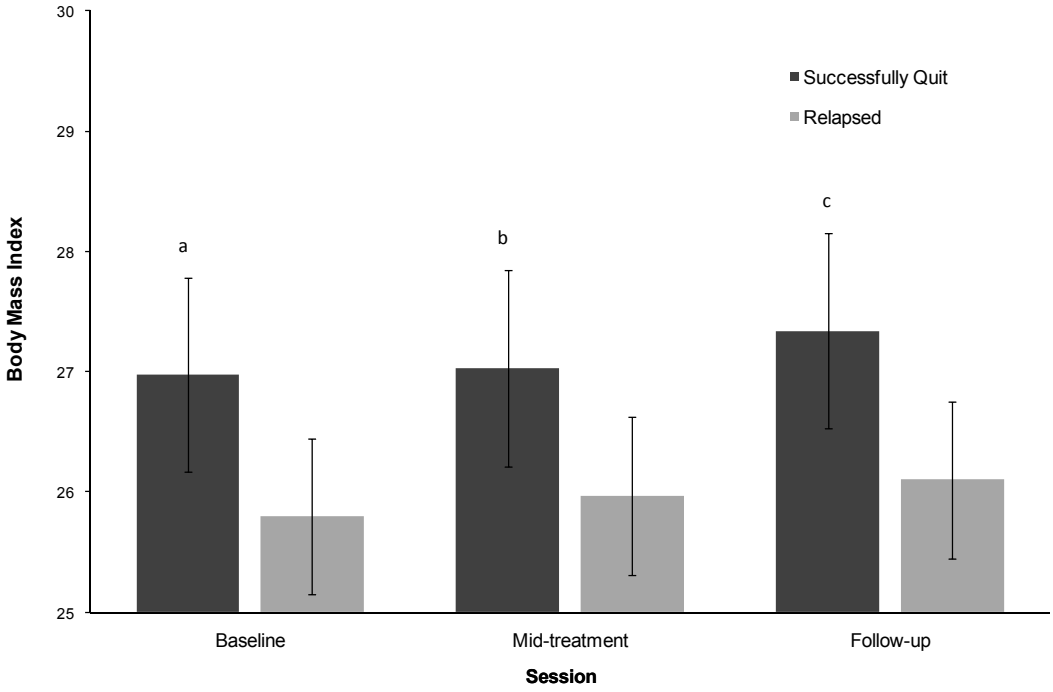

Figure 26. Changes in Body Mass Index for all Participants as a Function of Time. Bars represent mean values. Error bars represent standard errors of the means. Bars without common superscripts are statistically different from one another. There were no statistically significant across-session changes among those who relapsed.

Outcome measure	Successful quitters ($n = 20$)			Unsuccessful quitters ($n = 45$)			
	Mean*	(SE)*	[95% CI]*	Mean*	(SE)*	[95% CI]*	*P* value†
Systolic blood pressure							
Baseline	129.4	(3.01)	[19.91, 38.04]	131.5	(2.55)	[126.37, 136.56]	
Mid-treatment	125.1	(2.17)	[23.98, 37.24]	125.3	(1.84)	[121.58, 128.93]	.10
4-week follow-up	128.5	(2.13)	[25.17, 35.65]	122.7	(1.80)	[119.07, 126.25]	
Diastolic blood pressure							
Baseline	86.1	(3.38)	[79.27, 92.76]	87.2	(2.90)	[81.40, 92.99]	
Mid-treatment	83.4	(1.82)	[79.82, 87.08]	83.3	(1.56)	[80.16, 86.39]	.90
4-week follow-up	79.6	(1.40)	[76.78, 82.37]	79.0	(1.20)	[76.78, 82.37]	
Heart rate							
Baseline	79.9	(2.31)	[75.30, 84.54]	81.2	(1.99)	[77.21, 85.15]	
Mid-treatment	77.1	(2.04)	[73.00, 81.15]	79.8	(.23)	[76.30, 83.30]	.96
4-week follow-up	75.4	(1.76)	[71.93, 78.97]	76.4	(.22)	[73.42, 79.47]	
BMI							
Baseline	26.6	(.81)	[25.02, 28.25]	25.8	(.65)	[24.46, 27.06]	
Mid-treatment	27.0	(.82)	[25.39, 28.66]	26.0	(.66)	[24.67, 27.29]	.07
4-week follow-up	27.3	(.81)	[25.72, 28.96]	26.1	(.65)	[24.79, 27.40]	

Table 13. Summary of Results for Intent-to-Treat Analyses of Cardiovascular and Anthropometric Measures.

Abbreviations: BMI = body mass index; CI = confidence interval; SE = standard error.

*Adjusted for pack years, BMI, baseline activity level, baseline drinking severity, and smoking status at the mid-treatment evaluation.

†P value based on Greenhouse-Geisser adjustment for the interaction between group and time from analysis of variance (ANOVA) model covarying for pack years, BMI, baseline activity level, baseline drinking severity, and smoking status at the mid-treatment evaluation.

5.4.6 Post hoc analyses

Results of the linear regression analyses revealed no association between positive affect (PA) change scores (follow-up minus baseline) and erectile tumescence change scores for either successful ($r(18) = -.19$, $p = .41$, adj $R^2 = .02$) or unsuccessful quitters ($r(43) = -.22$, $p = .157$, adj $R^2 = .02$). Similarly, both successful ($r(18) = .10$, $p = .69$, adj $R^2 = .05$) and unsuccessful ($r(43) = .02$, $p = .90$, adj $R^2 = .02$) quitters displayed no association between negative affect (NA) change scores or between erectile tumescence change scores.

There was also no association between changes in PA or NA with respect to self-reported sexual arousal (PA for successful quitters: $r(18) = .17$, $p = .47$, adj $R^2 = .02$; PA for unsuccessful quitters: $r(43) = -.02$, $p = .92$, adj $R^2 = .02$; NA for successful quitters: $r(18) = .17$, $p = .47$, adj $R^2 = .02$; NA for unsuccessful quitters: $r(43) = -.02$, $p = .92$, adj $R^2 = .02$). Finally, there was no association between self-reported sexual functioning change scores and between changes in PA or NA (PA for successful quitters: $r(18) = .37$, $p = .11$, adj $R^2 = .09$; PA for unsuccessful quitters: $r(43) = -.03$, $p = .85$, adj $R^2 = .02$; NA for successful quitters: $r(18) = .09$, $p = .72$, adj $R^2 = .05$; NA for unsuccessful quitters: $r(43) = .03$, $p = .84$, adj $R^2 = .02$).

Taken together, these results indicate that there was no statistically significant relationship between across-session changes in mood and sexual health indices. Results of association between affect and each primary outcome variable for each group (successful quitters, relapsers) are summarized in Table 14.

Outcome measure	Successful quitters ($n = 20$)				Unsuccessful quitters ($n = 45$)			
	β	Adj R^2	t	p	β	Adj R^2	t	p
Physiological sexual arousal								
Positive affect	-.19	.02	-.84	.41	-.22	.02	-1.44	.16
Negative affect	.10	.05	.41	.69	.02	.02	.13	.90
Subjective sexual arousal								
Positive affect	.17	.02	.74	.47	-.02	.02	-.10	.92
Negative affect	-.01	.06	-.02	.99	.20	.02	1.31	.20
Self-reported sexual function*								
Positive affect	.37	.09	1.67	.11	-.03	.02	-.20	.85
Negative affect	.09	.05	.37	.72	.03	.02	.20	.84

Table 14. Results of Intent-to-Treat Analyses of Association between Affect and each Primary Outcome Measure.

CHAPTER 6: DISCUSSION

6.1 Overview

Cigarette smoking represents the most preventable cause of morbidity and mortality in the world today, and is responsible for enormous health-related economic burdens. Among other medical sequelae, erectile impairment has been shown to be associated with chronic tobacco use. Although quitting smoking substantially enhances many aspects of health, the positive health benefits of smoking cessation are not sufficient enough for many smokers to consider quitting (e.g., improvements in cardiovascular and pulmonary functioning, reduced risk of cancer). Therefore, the primary aim of this study was to provide the first empirical investigation of the effects of smoking cessation on physiological and subjective indices of sexual health, with the hope that the results would serve as a novel and enticing means to influence men to quit smoking.

6.2 Association between smoking cessation and physiological sexual arousal

It was hypothesized that men who successfully quit smoking, compared to those who relapsed, would display higher physiological sexual arousal responses at the 4-week follow-up compared to baseline (while smoking regularly), as a function of eliminating chronic nicotine and/or noxious pharmacological agents found within cigarettes. In concert with this hypothesis, results indicated that, at follow-up, abstinent men versus relapsed participants displayed: (i) significantly improved within-session raw changes in erectile tumescence; (ii) improved within-session percent changes in erectile tumescence;

and (iii) higher percent changes in maximum tumescence. In these cases, the magnitude of across-session changes in genital arousal was moderate (effect sizes ranging from .4 to .6); however, differential changes for successful versus unsuccessful quitters was small (effect sizes ranging from .2 to .3). With respect to time to reach maximum erection, there were no between-group differences at follow-up; however, abstinent versus relapsed participants demonstrated significant across-session improvements (from baseline to mid-treatment and from baseline to follow-up). Although successful quitters displayed improvements in both maximum tumescence and erectile onset as a result of quitting smoking, these across-session changes did not differ significantly from men who relapsed.

I also hypothesized that abstinent participants' physiological sexual arousal responses at mid-treatment would be intermediate to those assessed at baseline and follow-up. Despite these within-group graded improvements, I hypothesized that this would *not* translate to discernable between-group differences at mid-treatment. In line with these hypotheses, abstinent participants displayed a graded improvement across time for all physiological outcome variables; however, there were no statistical differences at mid-treatment between participants who quit smoking and those who relapsed.

Taken together, the overall pattern of results were similar to prior studies that have shown significant improvements in penile blood flow (Sighinolfi, et al., 2007), as well as rigidity and tumescence (Guay, et al., 1998), as a result of smoking cessation. Furthermore, results suggested that cessation-induced improvements in genital responses were attributable primarily to nicotine elimination (as evidenced by between-group

differences in physiological outcome measures at follow-up when successful quitters were nicotine/smoke free), rather than tobacco smoke discontinuation alone (i.e., lack of statistical between-group differences at mid-treatment). In other words, nicotine alone may indeed play a primary inhibitory role with respect to genital hemodynamic processes, thereby making men who were wearing the nicotine patch display similar results to men who were smoking (relapsed participants). In fact, effect sizes for between-group comparisons at follow-up (effect size range: .12 to .33) were approximately three times larger than the effect sizes for mid-treatment comparisons (effect size range: .01 to .09), suggesting that cessation of isolated nicotine versus cessation of tobacco smoke may serve as the chief factor in enhancing physiological arousal. These results are in line with prior results demonstrating that isolated nicotine hinders male genital responses (Harte & Meston, 2008b).

6.3 Association between smoking cessation and self-reported sexual arousal

Continuous levels of self-reported sexual arousal responses were used as an index of psychological sexual arousal during exposure to the erotic stimuli. Because men have a relatively salient physiological feedback system (i.e., erection) (Sakheim, et al., 1984), it is possible that over time – as a result of smoking-induced impaired erectile responses – smokers may synchronize their self-reported sexual arousal to match their inhibited genital arousal. Therefore, it was hypothesized that smokers would demonstrate the same across-session patterns of both subjective sexual arousal and physiological sexual arousal, and therefore subjective sexual arousal responses were expected to increase as a result of smoking cessation.

Although all participants demonstrated large and reliable increases in subjective sexual arousal during each experimental session, quitting smoking had no differential group effect on percent increase in self-reported sexual arousal or on latency to reach maximum subjective sexual arousal. There was, however, an association between quitting smoking and rate of onset to reach maximum subjective sexual arousal. Specifically, abstinent versus relapsed participants demonstrated significant across-session improvements (from baseline to follow-up and from mid-treatment to follow-up), resulting in between-group differences at follow-up. This suggested that men who were successfully smoke-free at follow-up demonstrated faster rates of feeling subjectively sexually aroused compared to unsuccessful quitters. In fact, at follow-up, successful quitters demonstrated a five-fold enhancement in rate of subjective sexual arousal compared to participants who relapsed (effect size = .50 vs .09).

To my knowledge, this is the first study that has examined the relationship between smoking cessation and subjective sexual arousal responses. Taken together, results indicated that, in some circumstances, quitting smoking is associated with improved self-reported sexual arousal. This is in line with well-established findings that male physiological and self-reported genital responses are correlated with one another (Chivers, Seto, Lalumiere, Laan, & Grimbos, 2009), and as such, facets of each domain may be improved accordingly by quitting smoking.

6.4 Association between smoking cessation and self-reported sexual functioning

A gold-standard self-report measure of sexual functioning was used as an ecologically valid way to assess changes in sexual health. As such, this measure

complemented the physiological laboratory assessments; it provided a mechanism to determine whether *statistically* significant improvements in physiological sexual arousal indices translated to *clinically* significant changes in sexual function, reflected in the participants' natural environments. It was hypothesized that sexual function would show a similar pattern of results compared to sexual arousal measured psychophysiologically. Specifically, it was hypothesized that erectile function, orgasmic function, intercourse satisfaction, and overall sexual function domains would be significantly higher at follow-up compared to both the pre-treatment and mid-treatment assessments. I also expected the same pattern of results with sexual desire and overall sexual satisfaction, but with uncertainty regarding statistical significance.

Although participants in most cases displayed improvements in sexual function domains (erectile function, orgasmic function, sexual desire, intercourse satisfaction, overall satisfaction) across time, successful quitters did not show a differential improvement compared to participants who relapsed. Similarly, there was no statistically significant association between quitting smoking and erectile dysfunction status at either mid-treatment or follow-up. However, it deserves mention that successful quitters demonstrated a 75% remission rate of ED, and at follow-up only 5% met criteria for ED, which is below age-associated norms (Laumann, et al., 1999; Selvin, et al., 2007). In fact, relapsed participants were nearly three times as likely to report ED at follow-up compared to successful quitters.

Taken together, results indicated that – unlike results of physiological and subjective sexual arousal – men did not show statistically significant improvements in

self-reported sexual functioning as a result of smoking cessation. There are a number of explanations that could account for this lack of discernable differences. First, it is possible that the statistical improvements in physiological arousal responses measured within the laboratory setting do not correspond to clinically significant enhancements that are discernable to participants in their natural environment. In other words, participant may have displayed subtle, albeit statistically significant, changes in erectile capacity that were not of sufficient magnitude to noticeably affect their sexual performances in real life sexual settings (e.g., penetration, erectile maintenance).

It is also possible that a 4-week follow-up period is not of sufficient length to fully capture improvements in sexual function that are associated with quitting smoking. It is feasible that quitting smoking enhances genital responses relatively quickly and in an automatic fashion, whereas men's perceptions of their sexual function (which is, in part, a result of partner feedback) may take longer to be reflected as significant augmentations via a self-report measure.

Finally, sexual function domain scores for successful quitters had quite large error variances relative to participants who relapsed. This was likely due to the fact that the subgroup of successful quitters (n = 20) was relatively small in size compared to unsuccessful quitters (n = 45). Although participants generally displayed improvements as a function of quitting smoking among sexual function domains, there was not sufficient power to detect these group×time interactions (post-hoc power range: .14 to .36).

6.5 Potential mechanisms of action

The results of the present study have interesting theoretical implications with respect to potential sexual arousal mechanisms that are affected by nicotine/tobacco. That participants showed increases in sexual arousal as a function of eliminating nicotine/tobacco intake, suggests that nicotine and/or cigarette constituents may deleteriously affect underlying components of the sexual arousal process in several ways. These individual pathways or interaction of pathways include: (i) central activation, by instigating neurotransmitter and/or neuroendocrine effects; (ii) peripheral activation, by facilitating SNS activation; or (iii) activation at the biochemical level, by targeting NO synthesis directly or indirectly. Complex interactions among these pathways may also exist (Sartori, et al., 2005).

Nicotine/tobacco affects the central nervous system by causing a cascading dose-related effect on physiological and biochemical functions (Pomerleau, 1992). After cigarette consumption, circulating levels of catecholamines increase, including a substantial increase in norepinephrine (Pomerleau & Pomerleau, 1985) (see Figure 27). Because norepinephrine is responsible for inhibiting erectile responses (Lincoln & Cornell, 1991), it is possible that chronic cigarette consumption reduces sexual arousal difficulties in men by attenuating circulating norepinephrine to normal levels, thereby facilitating an optimal biochemical environment for adequate genital hemodynamic responses. This notion is supported by research indicating that chronic nicotine exposure

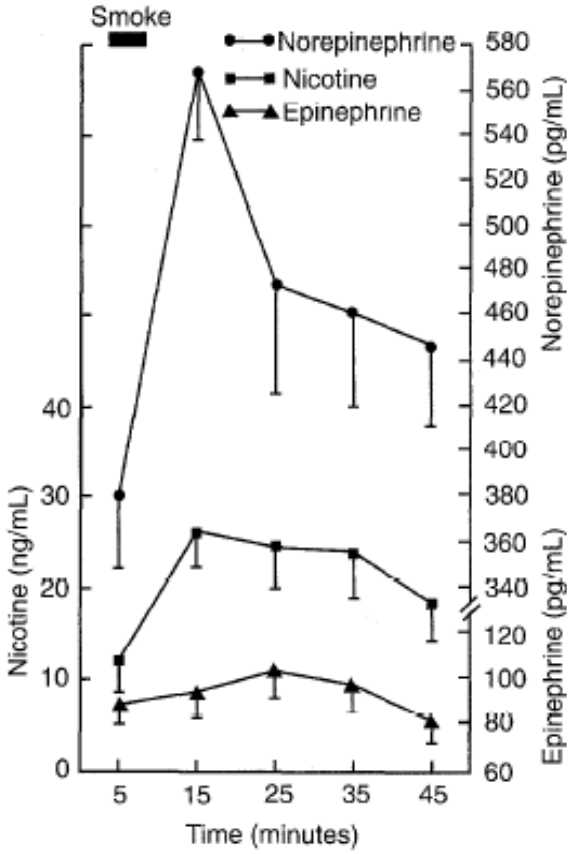

Figure 27: Patterns of Change in Serum Norepinephrine and Epinephrine Levels Relative to Nicotine Concentrations Resulting from a Nicotine Exposure.

Note: approximately 1 mg nicotine content. Mean (+SEM) for 10 smokers who smoked following a 1.5-hour interval without cigarettes. Figure from (Pomerleau, 1992).

has deleterious effects on modulating the balance between adrenaline and noradrenaline (Jeremy & Mikhailidis, 1998).

The disinhibition of physiological sexual arousal following smoking cessation is consistent with literature delineating nicotine's effects on SNS activity. Specifically, nicotine causes cardiovascular constriction (increased heart rate and blood pressure,

increased myocardial contractibility) and is primarily responsible for maintaining erectile flaccidity (Dean & Lue, 2005). Thus, the enhancement of physiological sexual arousal subsequent to the elimination of tobacco smoke and/or nicotine, may be the result of the PNS and SNS operating in a relatively more balanced fashion, thereby facilitating conditions for optimal erectile responses.

Quitting smoking may also directly impact biochemical processes underlying erection physiology. It has been proposed that free radicals and other compounds within cigarettes may decrease the endothelial synthesis of nitric oxide (NO) directly, or indirectly by targeting precursors (disrupting the activity of eNOS thereby disrupting the conversion of L-arginine to NO), resulting in decreased penile blood inflow (McVary, et al., 2001; Zhang, et al., 2006). Considering that NO has been identified as the principal neurotransmitter mediating erection (Burnett, et al., 1992; Kim, et al., 1991), it is possible that the elimination of both nicotine and tobacco smoke relieves the disruption of endothelial synthesis of NO, resulting in enhanced smooth muscle relaxation, vasocongestion, and improved erectile response. Another potential pathway that may be responsible for inhibiting penile hemodynamic processes is the role of smoking-generated carbon monoxide (CO). It has been shown that both exogenous and endogenously formed CO can instigate endothelium-dependent vasoconstriction by inhibiting endothelial NO formation (Johnson & Johnson, 2003).

An interesting finding was that there were no differences in physiological sexual arousal between participants using a high-dose nicotine patch and participants who were smoking cigarettes (i.e., there were no between-group differences at mid-treatment).

Furthermore, it was not until participants discontinued the nicotine patch that they exhibited significant improvements in sexual health, as compared to when they discontinued smoking and wore a nicotine patch. This may suggest that pharmacologically active non-nicotine ingredients found within cigarettes have a relatively weaker inhibiting effect on sexual arousal compared to nicotine alone. However, it should be noted that without measuring the concentration of the drug *in vivo* (via plasma nicotine or plasma cotinine (a by-product of nicotine)) and then covarying for these concentrations across conditions, it is impossible to know with certainty which nicotine delivery method exerts a more deleterious effect on physiological processes underlying sexual arousal.

The aforementioned theories on the mechanisms of action of nicotine and tobacco smoke on sexual arousal are purely speculative. At present, this complex interaction of biochemical, physiological, and psychological mechanisms underlying the sexual response process are still not entirely understood. More research at the basic science level is needed in order to elucidate the pharmacological role of cigarette smoking on male (and female) sexual health.

6.6 Strengths

The present study has several strengths. First, to my knowledge, this is the first study examining sexual function and smoking cessation that recruited men irrespective of ED status. This is especially important, considering that the majority of smokers (under

60 years of age[‡]) would not be expected to have erectile difficulties. Including men both with and without ED enables the results to generalize to a significantly larger population of men.

Second, this is the first study to examine changes in sexual health as a result of quitting smoking using several physiological indices. Incorporating a variety of genital measures provided a way to capture a well-defined and multifaceted overall picture of the changes in the penile hemodynamic process.

Third, the present investigation is the first to examine changes in sexual health via a self-report measure. Complementing physiological laboratory assessments with a well-validated self-report measure of sexual functioning provided a means of assessing *clinically* significant changes. Moreover, including measures of continuous subjective sexual arousal responses provided a means to assess the interplay between cognitive appraisal of the erotic stimuli and physiologic responses.

Fourth, this is the first study to examine smoking cessation and sexual health using a follow-up period of intermediate length (4 weeks). Previous studies have tested men 24 to 36 hours after quitting "cold turkey," and therefore, it is reasonable to believe that both physiological and psychological nicotine withdrawal effects could have affected results.

[‡] After 60 years of age, the natural age-associated rate of ED increases substantially, with the majority of individuals reporting clinically significant erectile difficulties (Laumann, et al., 1999; Martin-Morales, et al., 2001; Selvin, et al., 2007).

Fifth, this was the first study examining the association between quitting smoking and sexual health that has included a comparison control group (relapsed participants), thereby enhancing internal validity.

6.7 Limitations

There are a number of limitations of this study that warrant mention. The most important limitation is in regard to the study methodology. This was not a clinical trial with randomization. The study did, however, use a between-group design, comparing relapsed participants (which served as a quasi-control group) to successful quitters; however the relapsed group was quite heterogeneous in nature. That is, this group comprised individuals who differed in severity of relapse (i.e., full relapse, or partial lapse), as well as in timing of relapse (i.e., at the outset of treatment, final week prior to the follow-up evaluation). Several statistical steps were taken to ensure adequate between-group similarity; however without *random* group assignments and without a bonafide waitlist control condition, one cannot rule out several potential confounding factors. For this study the most applicable threats to internal validity would have been effects of testing and instrumentation (Kirk, 2009), as well as regression toward the mean (Nesselroade, Stigler, & Baltes, 1980).

I believe that instrumentation effects (e.g., lack of adequate calibration of equipment) would have been minimal, as all equipment was calibrated after each use. I believe that regression effects (e.g., a patient seeks help while in an extreme clinical

state[§]) would be minimal as well. This was suspected for three reasons: (i) first, one would not expect ED to spontaneously remit like other psychological disorders (e.g., major depressive disorder); (ii) second, all participants self-referred because they wanted to quit smoking, not because they wanted to see improvements in sexual health; and (iii) third, only the minority of participants reported erectile difficulties of a clinical nature.

The possibility of a potential testing effect (i.e., practice effects, fatigue, habituation, sensitization) deserves further mention. It is possible that participants may have become either more sensitive to the erotic stimuli and/or more relaxed during each subsequent session (e.g., less anxiety, less distracting performance-evaluative thoughts), which could have resulted in higher sexual arousal at follow-up, thus masking the effects of the treatment intervention. I could find no literature documenting the effect of across-trial sensitization in male genital responding to erotic cues. Rather, literature points to habituation effects in some circumstances. Specifically, it has been shown that men display significantly reduced physiological and subjective sexual arousal responses to the same erotic stimulus both within- and across- trials (O'Donohue & Plaud, 1991; Plaud, Gaither, Henderson, & Devitt, 1997). However, men do not show differences in either physiological or subjective sexual arousal either within- or across- experimental sessions when the stimuli are varied (O'Donohue & Plaud, 1991; Plaud, et al., 1997). Because the current study incorporated varied erotic stimuli to which participants were counterbalanced, one should not expect any association between testing effects and sexual arousal (either habituation or sensitization). Furthermore, it should be noted that

[§] In this case, an extreme state of ED.

changes in affect did not covary with any of the primary outcome variables, indicating that increases in sexual health were in fact due to the removal of nicotine and tobacco-smoke which were likely responsible for causing deleterious effects on erectile hemodynamic responses. Finally, because between-group statistical differences were found with respect to both physiological and sexual arousal outcome measures, this suggests that testing effects were minimal at best.

A second limitation is that smoking abstinence was determined by self-report rather than by biochemical verification (e.g., expired air carbon monoxide, thiocyanate (SCN), serum nicotine, serum cotinine). As such, it is impossible to determine whether participants accurately reported their cigarette use. It should be noted that all participants provided saliva samples at each visit and were spuriously informed that these samples would be assayed for cotinine content (a byproduct of nicotine that has a relatively long half-life), and verified with their self-report (i.e., the bogus pipeline technique (Jones & Sigall, 1971)). This technique has been shown to produce reliable and accurate estimates of smoking (Murray, O'Connell, Schmid, & Perry, 1987). In studies in which participants have actually been asked to provide biochemical samples prior to reporting their smoking levels, little underreporting has generally been found (Bauman & Dent, 1982; Luepker, et al., 1981; Pechacek, et al., 1984). Additionally, in a meta-analysis that examined the concordance between self-reported smoking and biological verification of smoking activity (N = 36,830), it was determined that self reports of smoking were quite accurate (Patrick, et al., 1994).

A third limitation is with respect to the dropout rate; only 53% of participants completed the follow-up session. In order to address this issue, several steps were taken to ensure the reliability of the observed effects. As such, data were analyzed using list-wise deletion, last observation carried forward (LOCF), and with missing data estimation (full information maximum likelihood (FIML)). In fact, FIML is considered a ‘‘state-of-the-art’’ approach (J.L. Schafer & Graham, 2002) and has been shown to produce more accurate parameter estimates than either list-wise deletion or LOCF (Enders, 2001; Enders & Bandalos, 2001; J.L. Schafer & Graham, 2002). Additionally, Little and Rubin (2002) and Schafer (1997) have both suggested that data estimation methods using FIML can reliably be used when up to 90% of the data are missing for a particular variable.

The formulation of outcome groups (abstinent vs. relapsed) also deserves mention. Because completely abstinent men (zero cigarettes during a 7-day point prevalence) and partially abstinent men (0 to 3 cigarettes/day during 7-day point prevalence) did not show any differences with respect to their changes in sexual health as a function of smoking cessation, these two groups were combined for the initial analyses among the subgroup of successful smokers. As such, this entire group was considered “nonsmokers.” Although results show that significantly reducing tobacco consumption (but not completely eliminating smoking) significantly enhances sexual health, this should in no way be interpreted to mean that smoking 1 to 3 cigarettes per day poses no health hazards. Although the risk of cancer decreases in a dose-dependent fashion with reduction in smoke exposure, individuals smoking a few cigarettes per day still have a nearly 5-fold risk of cancer (U.S. Department of Health and Human Services, 1989).

Furthermore, smoking even a few cigarettes per day increases the risk of heart disease mortality (Bjartveit & Tverdal, 2005) and respiratory diseases (Bohadana, Nilsson, Westin, Martinet, & Martinet, 2006) nearly as much as smoking a pack per day. With these data in mind, all individuals should aim to be completely abstinent.

Another limitation is with respect to the sample size. Although this study used a repeated-measures design, which enhances statistical power, the sample sizes of the outcome groups for the intent-to-treat analyses were still relatively low, especially for the subgroup of successful quitters (n = 20). Thus, there was not sufficient power to detect several group×time interactions, particularly for sexual function measures (post-hoc power range: .14 to .36).

The generalizability of the sample is also another potential limitation of this study. Considering that this study was sexual in nature, biases among participants participating in sexuality research should also be considered. Specifically, compared to non-volunteers, those who self-select for sexuality research tend to be more sexually experienced, have less traditional sexual attitudes, endorse greater sexual sensation seeking, and are more interested in sexually explicit materials (Brecher & Brecher, 1986; D. Saunders, Fisher, Hewitt, & Clayton, 1985; Wiederman, 1999; Wolchik, Braver, & Jensen, 1985).

In this study, erectile dysfunction was assessed via a self-report measure, and therefore participants did not undergo a clinical evaluation in order to be diagnosed according to medical guidelines (i.e., DSM-IV-TR or ICD-10 (World Health Organization, 1993)). Considering that classification of ED in this study was to serve as a

primary endpoint, rather than understanding the etiology and type of erectile difficulty, using the IIEF seemed quite appropriate. Furthermore, the IIEF has been adopted as the "gold standard" measure for brief evaluation of self-reported erectile functioning and has been used in more than 50 clinical trials (RC Rosen, Cappelleri, & Gendrano, 2002).

6.8 Clinical implications

The results of this study have important clinical implications. Results have the possibility to serve as an important mechanism to enhance men's interest and commitment to quit smoking, considering that they may show an increase in erection, as well as increases in subjective sexual arousal. Simply stated, if men do not want to quit smoking for their heart or for their lungs, perhaps they would consider quitting for increased sexual performance. In addition to discussing traditional acute (e.g., enhanced cardiovascular and pulmonary functioning) and long-term (e.g., reduced morbidity and mortality from cancer, lung disease, and heart disease) benefits of quitting smoking with patients, healthcare providers may find it useful to discuss the acute benefits of quitting smoking in terms of increased erectile performance.

These results may also have implications for therapeutic patient screening. It has been shown that providing patients with feedback on adverse changes associated with smoking can increase the salience of the negative impact of smoking to patients' health and consequently improve quit rates (Bovet, Perret, Cornuz, Quilindo, & Paccaud, 2002). As such, patients may benefit from receiving feedback of their actual erectile responses while smoking, and again pre- and post NRT. This "scientific evidence" that they are showing improvements in sexual health may serve as an important motivation to continue

with the cessation process, as well as maintain their newly acquired smoke-free lifestyle. This would likely increase self-efficacy, confidence, and autonomy, all of which are associated with successful cessation (Williams, Gagné, Ryan, & Deci, 2002).

These results are widely generalizable in that these data hold for heavy smoking men aged 23-60, irrespective of self-reported erectile difficulties. That is, even men who do not complain of erectile problems may still benefit sexually from quitting smoking. In fact, evidence suggests that smoking may have a stronger deleterious effect on sexual functioning in young male smokers compared to older male smokers (Gades, et al., 2005). Therefore, these results may serve as an important motivator – particularly for young men who may put considerable importance on their erectile performance – to consider quitting smoking.

A final point to mention is that the laboratory-assessed changes in genital arousal did not corresponded to noticeable enhancements in sexual function. That is, the data do not necessarily suggest that quitting smoking is a feasible way to treat ED (at least in the short-term). Rather, it is hoped that these *statistical* findings of cessation-induced sexual health enhancements may ultimately promote men to quit smoking. Therefore, the data may serve as a novel means to alleviate smoking-associated morbidity and mortality.

6.9 Public health implications

Although the rate of cigarette smoking is declining in the Unites States, it is still not nearly sufficient to meet the National Health Service's objective to reduce the prevalence of cigarette smoking among adults to <12% (Centers for Disease Control and Prevention, 2006). The public health burden due to smoking is enormous. There are

approximately 1 billion current smokers worldwide, causing an estimated 200 billion in economic damages each year based on the costs to treat tobacco-related illnesses and the indirect costs associated with disability (Zaher, Halbert, Dubois, George, & Nonikov, 2004). The worldwide death toll from smoking is expected to rise from 5 million to 10 million people per year by the year 2030 (Ezzati & Lopez, 2003), and the World Health Organization anticipates that tobacco will become the largest single health problem by the year 2020 (Vainio, Weiderpass, & Kleihues, 2001). With these alarming statistics in mind, help from all sources is needed in order to ameliorate the negative impact of cigarette smoking on health.

It is hoped that the results of the present study may serve as a novel means to facilitate programs and interventions targeting the prevention and cessation of cigarette smoking in men. In particular, these results have the potential to influence practitioners to discuss with male patients the benefits of starting the quitting process. Enhancing successful smoking cessation in men would significantly enhance quality of life, substantially reduce premature death, and alleviate enormous economic burdens caused by smoking-related diseases such as cardiovascular disease, respiratory disease, and cancer. Moreover, facilitating patients to quit smoking not only enhances their own quantity and quality of life, but also improves the long-term health of patients' families and friends. In fact, approximately 40,000 nonsmokers in the United States die prematurely each year due to secondhand smoke exposure (Centers for Disease Control and Prevention, 2005).

6.10 Conclusions

The results of the present investigation provide the first empirical evidence that smoking cessation significantly enhances both physiological and self-reported indices of sexual health in long-term male smokers, irrespective of baseline erectile impairment. These results have the potential for facilitating programs and interventions targeting the prevention and cessation of cigarette smoking in men.

APPENDIX A

International Index of Erectile Function

Rosen, Riley, Wagner, Osterloh, Kirkpatrick, & Mishra (1997)

INSTRUCTIONS: These questions ask about your sexual feelings and responses during the past 4 weeks. Please answer the following questions as honestly and clearly as possible. Your responses will be kept completely confidential. Check only one box per question

1. Over the past 4 weeks, how often were you able to get an erection during sexual activity?
   - 1 = Almost never/never
   - 2 = A few times (much less than half the time)
   - 3 = Sometimes (about half the time)
   - 4 = Most times (much more than half the time)
   - 5 = Almost always/always
   - 0 = No sexual activity

2. Over the past 4 weeks, when you had erections with sexual stimulation, how often were your erections hard enough for penetration?
   - 1 = Almost never/never
   - 2 = A few times (much less than half the time)
   - 3 = Sometimes (about half the time)
   - 4 = Most times (much more than half the time)
   - 5 = Almost always/always
   - 0 = Did not attempt intercourse

3. Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?
   - 1 = Almost never/never
   - 2 = A few times (much less than half the time)
   - 3 = Sometimes (about half the time)
   - 4 = Most times (much more than half the time)
   - 5 = Almost always/always
   - 0 = Did not attempt intercourse

4. Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
   - 1 = Almost never/never
   - 2 = A few times (much less than half the time)
   - 3 = Sometimes (about half the time)
   - 4 = Most times (much more than half the time)
   - 5 = Almost always/always
   - 0 = Did not attempt intercourse

5. Over the past 4 weeks, during sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
    1 = Extremely difficult
    2 = Very difficult
    3 = Difficult
    4 = Slightly difficult
    5 = Not difficult
    0 = Did not attempt intercourse

6. Over the past 4 weeks, how many times have you attempted sexual intercourse?
    1 = One to two attempts
    2 = Three to four attempts
    3 = Five to six attempts
    4 = Seven to ten attempts
    5 = Eleven + attempts
    0 = No attempts

7. Over the past 4 weeks, when you attempted sexual intercourse, how often was it satisfactory?
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always
    0 = Did not attempt intercourse

8. Over the past 4 weeks, how much have you enjoyed sexual intercourse?
    1 = No enjoyment
    2 = Not very enjoyable
    3 = Fairly enjoyable
    4 = Highly enjoyable
    5 = Very highly enjoyable
    0 = No intercourse

9. Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you ejaculate?
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always
    0 = No sexual stimulation/intercourse

10. Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always
    0 = No sexual stimulation/intercourse

11. Over the past 4 weeks, how often have you felt sexual desire?
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always

12. Over the past 4 weeks, how would you rate your level of sexual desire?
    1 = Very low/none at all
    2 = Low
    3 = Moderate
    4 = High
    5 = Very high

13. Over the past 4 weeks, how satisfied have you been with your overall sex life?
    1 = Very dissatisfied
    2 = Moderately dissatisfied
    3 = About equally satisfied and dissatisfied
    4 = Moderately satisfied
    5 = Very satisfied

14. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?
    1 = Very dissatisfied
    2 = Moderately dissatisfied
    3 = About equally satisfied and dissatisfied
    4 = Moderately satisfied
    5 = Very satisfied

15. Over the past 4 weeks, how do you rate your confidence that you could get and keep an erection?
    1 = Very low
    2 = Low
    3 = Moderate
    4 = High
    5 = Very high

Scoring:

Domain	Items	Score Range	Min score	Max score
EF	1,2,3,4,5,15	0 (or 1) – 5	1	30
OF	9,10	0-5	0	10
SD	11,12	1-5	2	10
IS	6,7,8	0-5	0	15
OS	13,14	1-5	2	10

EF = erectile function, OF = orgasmic function, SD = sexual desire, IS = intercourse satisfaction, OS = overall satisfaction

APPENDIX B

Kinsey Sexual Orientation Scale

Kinsey, Pomeroy, & Martin (1948)

Based on both psychological reactions and overt experience, rate yourself as one of the following:

0. Exclusively heterosexual with no homosexual
1. Predominantly heterosexual, only incidentally homosexual
2. Predominantly heterosexual, but more than incidentally homosexual
3. Equally heterosexual and homosexual
4. Predominantly homosexual, but more than incidentally heterosexual
5. Predominantly homosexual, only incidentally heterosexual
6. Exclusively homosexual

APPENDIX C

Alcohol Use Disorders Identification Test

Saunders, Aasland, Babor, de la Fuente, & Grant (1993)

Box 4

The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct answer number in the box at the right.

1. How often do you have a drink containing alcohol?
   (0) Never [Skip to Qs 9-10]
   (1) Monthly or less
   (2) 2 to 4 times a month
   (3) 2 to 3 times a week
   (4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   (0) 1 or 2
   (1) 3 or 4
   (2) 5 or 6
   (3) 7, 8, or 9
   (4) 10 or more

3. How often do you have six or more drinks on one occasion?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
   Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0

4. How often during the last year have you found that you were not able to stop drinking once you had started?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?
   (0) No
   (2) Yes, but not in the last year
   (4) Yes, during the last year

10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?
    (0) No
    (2) Yes, but not in the last year
    (4) Yes, during the last year

Record total of specific items here

If total is greater than recommended cut-off, consult User's Manual.

APPENDIX D

Drug Abuse Screening Test

Skinner, 1982

DAST-10©

The questions included in the DAST-10 concern information about possible involvement with drugs not including alcoholic beverages during the past 12 months.

In the statements, "drug use" refers to (1) the use of prescribed or over the counter drugs in excess of the directions and (2) any non-medical use of drugs. The various classes of drugs may include: cannabis (marijuana, hashish), solvents, tranquilizers (e.g., Valium), barbiturates, cocaine, stimulants (e.g., speed) hallucinogens (e.g., LSD) or narcotics (e.g., heroin).

In the past 12 months:	*Circle response*	
1. Have you used drugs other than those required for medical reasons?	Yes	No
2. Do you abuse more than one drug at a time?	Yes	No
3. Are you always able to stop using drugs when you want to?	Yes	No
4. Have you had "blackouts" or "flashbacks" as a result of your drug use?	Yes	No
5. Do you ever feel bad or guilty about your drug use?	Yes	No
6. Does your spouse (or parents) ever complain about your involvement with drugs?	Yes	No
7. Have you neglected your family because of your use of drugs?	Yes	No
8. Have you engaged in illegal activities in order to obtain drugs?	Yes	No
9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?	Yes	No
10. Have you had medical problems as a result of your drug use (e.g., memory loss, hepatitis, convulsions, bleeding, etc.)?	Yes	No

APPENDIX E

Fagerstrom Test for Nicotine Dependence

Heatherton, Kozlowski, Frecker, & Fagerstrom (1997)

1. How soon after you wake up do you smoke your first cigarette?
   - ☐ After 60 minutes (0)
   - ☐ 31-60 minutes (1)
   - ☐ 6-30 minutes (2)
   - ☐ Within 5 minutes (3)

2. Do you find it difficult to refrain from smoking in places where it is forbidden?
   - ☐ No (0)
   - ☐ Yes (1)

3. Which cigarette would you hate most to give up?
   - ☐ The first in the morning (1)
   - ☐ Any other (0)

4. How many cigarettes per day do you smoke?
   - ☐ 10 or less (0)
   - ☐ 11-20 (1)
   - ☐ 21-30 (2)
   - ☐ 31 or more (3)

5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?
   - ☐ No (0)
   - ☐ Yes (1)

6. Do you smoke even if you are so ill that you are in bed most of the day?
   - ☐ No (0)
   - ☐ Yes (1)

0-2 Very low dependence
3-4 Low dependence
5 Medium dependence
6-7 High dependence
8-10 Very high dependence

APPENDIX F

Positive and Negative Affect Schedule

Watson, Clark, & Tellegen (1988)

This scale consists of a number of words that describe different feelings and emotions. Read each item and then circle the appropriate number that indicates to what extent you feel this way right now.

		very slightly or not at all	a little	moderately	quite a bit	extremely
1.	**interested**	1	2	3	4	5
2.	**distressed**	1	2	3	4	5
3.	**excited**	1	2	3	4	5
4.	**upset**	1	2	3	4	5
5.	**strong**	1	2	3	4	5
6.	**guilty**	1	2	3	4	5
7.	**scared**	1	2	3	4	5
8.	**hostile**	1	2	3	4	5
9.	**enthusiastic**	1	2	3	4	5
10.	**proud**	1	2	3	4	5
11.	**irritable**	1	2	3	4	5
12.	**alert**	1	2	3	4	5
13.	**ashamed**	1	2	3	4	5
14.	**inspired**	1	2	3	4	5
15.	**nervous**	1	2	3	4	5
16.	**determined**	1	2	3	4	5
17.	**attentive**	1	2	3	4	5
18.	**jittery**	1	2	3	4	5
19.	**active**	1	2	3	4	5
20.	**afraid**	1	2	3	4	5

APPENDIX G

Systematic Assessment for Treatment Emergent Events

Levine & Schooler (1986)

SAFTEE

Identification #:_____ **Sequence:** 4 week check (2nd Session) 8 week check **Date:**_____

Instructions: Complete for all visits for patients who are assigned to MM. For further instructions, see ***Safety Guidelines*** **Part 1** and **2** (Forms A-8 and A-8).

Question	Event	Date of Onset	Duration (Days)	Pattern	Severity	Drug Related	Action Taken
				IS IN CO	MN MI MO S	N DR TO K O X	N IS C SU DC O R I
A. General Inquiry							
Have you had any physical or health problems since your last visit?	1	1	1	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	2	2	2	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
Have you noticed any changes in your physical appearance since your last visit?	3	3	3	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	4	4	4	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	5	5	5	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
Have you cut down on the things you usually do because you have not felt well physically since your last visit?	6	6	6	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	7	7	7	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	8	8	8	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	9	9	9	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
	10	10	10	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
				IS = Isolated IN = Intermittent CO = Continuous	MN = Minimal MI = Mild MO = Moderate S = Severe	N = No DR = Dose Response TO = Timing of Onset K = Known drug effect O = Other (specify) X = Don't know	N = None IS = Increased surveillance C = Contra active RX SU = Suspend RX DC = Discontinue RX O = Other R = Dose Reduction I = Dose Increased

Question	Event	Date of Onset	Duration (Days)	Pattern	Severity	Drug Related	Action Taken
				IS IN CO	MN MI MO S	N DR TO K O X	N IS C SU DC O R I
B. Specific Events Have you had any of the following problems since your last visit?	Prev/Rec Y N						
1. Nausea	☐ ☐ ☐	1 ____	1 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
2. Vomiting	☐ ☐ ☐	2 ____	2 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
3. Diarrhea	☐ ☐ ☐	3 ____	3 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
4. Abdominal Pain	☐ ☐ ☐	4 ____	4 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
5. Decreased Appetite	☐ ☐ ☐	5 ____	5 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
6. Increased Appetite	☐ ☐ ☐	6 ____	6 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
7. Headache	☐ ☐ ☐	7 ____	7 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
8. Dizziness	☐ ☐ ☐	8 ____	8 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
9. Fatigue	☐ ☐ ☐	9 ____	9 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
10. Nervousness/anxiety	☐ ☐ ☐	10 ____	10 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
11. Insomnia	☐ ☐ ☐	11 ____	11 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
12. Somnolence	☐ ☐ ☐	12 ____	12 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
13. Depression*	☐ ☐ ☐	13 ____	13 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
14. Itching	☐ ☐ ☐	14 ____	14 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
15. Rash	☐ ☐ ☐	15 ____	15 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
16. Decreased Libido	☐ ☐ ☐	16 ____	16 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
17. Increased Libido	☐ ☐ ☐	17 ____	17 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
18. Missed Menses	☐ ☐ ☐	18 ____	18 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
19. Significant lab abnormalities (describe)	☐ ☐ ☐	19 ____	19 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
20. Other (describe)	☐ ☐ ☐	20 ____	20 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
21. Other (describe)	☐ ☐ ☐	21 ____	21 ____	☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
*Requires additional specification				IS = Isolated IN = Intermittent CO = Continuous	MN = Minimal MI = Mild MO = Moderate S = Severe	N = No DR = Dose Response TO = Timing of Onset K = Known drug effect O = Other (specify) X = Don't know	N = None IS = Increased surveillance C = Contra active RX SU = Suspend RX DC = Discontinue RX O = Other R = Dose Reduction I = Dose Increased

APPENDIX H

Participant Feedback Report

The Sexual Psychophysiology Laboratory
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QUIT SMOKING STUDY - Health Feedback Report

Name:
Study ID#: SCS32
Age: 43

Date of Visit 1: 7/1/2009
Date of Visit 2: 7/23/2009
Date of Visit 3: 9/24/2009

Patch treatment length: 7 weeks
Dosage regimen: 21mg (3 weeks); 14mg (3 weeks), 7mg (1 week)

Physical Measures

	Visit 1	Visit 2	Visit 3	Change from Baseline:
Weight (lbs)	161.40	158.40	159.60	-1.80
Height (in.)	77.00	77.00	77.00	0.00
BMI (kg/m^2)	18.78	18.43	18.57	-0.21

Cardiovascular Measures

	Visit 1	Visit 2	Visit 3	Change from Baseline:
Systolic Blood Pressure (mm Hg)	116	129	121	5
Diastolic Blood Pressure (mm Hg)	82	80	63	-19
Heart Rate (BPM)	87	76	91	4

Sexual Functioning*

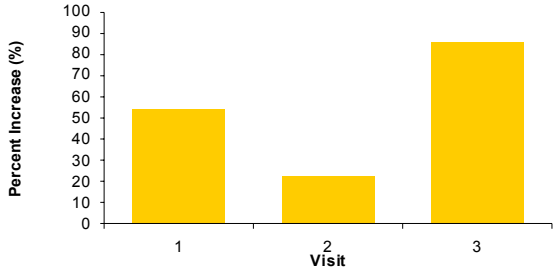
*Based on the 15 item self-report questionnaire

	Visit 1	Visit 2	Visit 3	Change from Baseline:
Arousal	29	27	29	0
Orgasm	7	8	10	3
Desire	10	8	8	-2
Sexual Satisfaction	12	10	13	1
Overall Satisfaction	10	9	10	0

Sexual Arousal (Self-Reported)†

†Recorded continuously with an optical mouse

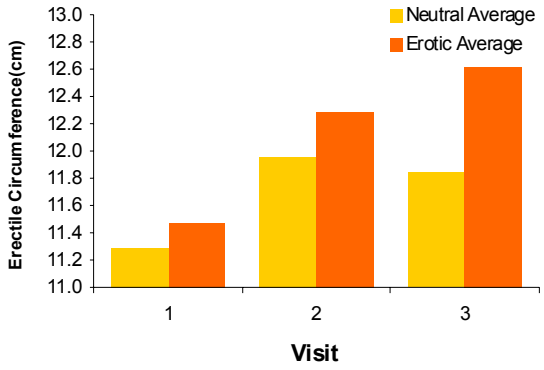
	Visit 1	**Visit 2**	**Visit 3**	Change from Baseline:
Percent Increase¶	53.9731211	22.52607	86.04038	32.07



¶ Calculated as the percent increase from the mean arousal during the neutral film segment to the mean arousal during the erotic film segment

Sexual Arousal (Physiological) - Mean penile circumference

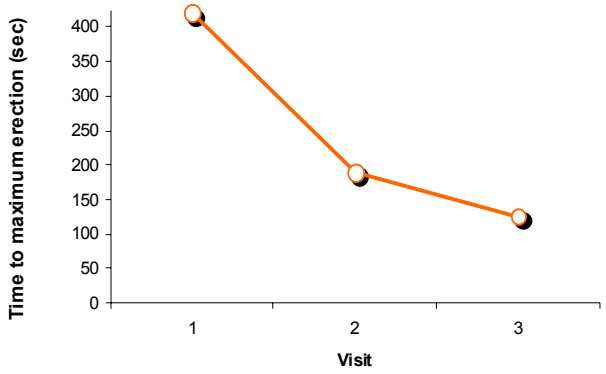
	Visit 1		Visit 2		Visit 3	
	Neutral	Erotic	Neutral	Erotic	Neutral	Erotic
Mean Circumference (cm)¶	11.2770724	11.46964	11.96363	12.2859	11.83583	12.61859



¶ Calculated as the mean circumference during the neutral film segment and the mean circumference during the erotic film segment

Sexual Arousal (Physiological) - Time to maximum erection

	Visit 1	Visit 2	Visit 3	Change from Baseline:
Time (seconds)	420.00	189.00	126	-294.00



Interpretive Report

BMI – Body mass Index is a statistical measurement which compares a person's weight and height. Though it does not actually measure the percentage of body fat, it is a useful tool to estimate a healthy body weight based on how tall a person is.

Over the course of the study, you have lost 1.8lbs. Based on your current BMI of 18.57 you are currently within the normal weight range.

Blood Pressure - For each heartbeat, blood pressure varies between systolic and diastolic pressures. Systolic pressure is peak pressure in the arteries. Diastolic pressure is minimum pressure in the arteries, which occurs near the beginning of the cardiac cycle when the ventricles are filled with blood.

Over the course of the study, your systolic Blood pressure increased by 5 units and your diastolic blood pressure decreased by 19 units. Your current blood pressure of 121/63 is currently within the normal range.

Heart Rate - is a measure of the number of heart beats per minute (bpm). The average resting human heart rate is about 70 bpm for adult males and 75 bpm for adult females.

Over the course of the study, your heart rate increased by 4 bpm. Your current heart rate of 91 bmp is currently within the normal range.

Sexual Functioning - Level of sexual functioning was assessed at each session with the International Index of Erectile Function (IIEF). The IIEF is the most widely used index of erectile function and is a 15-item measure assessing five-factor areas of male sexual functioning: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.

Over the course of the study, your erectile function score remained unchanged; your orgasmic function score remained increased by 3 points; your sexual desire score decreased by 2 points; your sexual satisfaction score increased by 1 point; and your overall satisfaction score remained unchanged. Overall, your self-reported sexual functioning slightly improved from baseline to follow-up.

Self-Reported Sexual Arousal - Continuous subjective sexual arousal was measured using a hand-controlled device which consisted of a computer optical mouse mounted on a wooden track divided into seven equally spaced intervals, where 0 indicated neutral, and 1–7 reflected increasingly higher levels of feeling sexually aroused. Sexual arousal was calculated within each session as the percent increase from the mean arousal during the neutral film segment to the mean arousal during the erotic film segment.

Over the course of the study, your self-reported sexual arousal increased by 32 percentage units.

Physiological Sexual Arousal – genital sexual arousal was assessed via penile circumferential change using a mercury-in-rubber strain gauge positioned mid-shaft on the penis. Physiological sexual arousal was calculated as the circumferential change in cm from the mean arousal during the neutral film segment to the mean arousal during the erotic film segment. Physiological sexual arousal was also measured by calculating the amount of time to reach your maximum erection during each visit.

Over the course of the study, your physiological sexual response significantly increased.

Additionally, the amount of time to reach your maximal erection decreased by 294 seconds. This indicates that you are now able to reach your maximum erection in less time compared to when you were smoking (during visit 1).

Overall Summary of Results: Throughout the course of the study, you showed an increase in cardiovascular health as demonstrated by your lowered blood pressure. Furthermore, your physical health improved as you lost 1.8lbs and your BMI score decreased. You had a slight increase in self-reported sexual functioning. Finally, you showed a significant increase in self-reported sexual arousal and physiological sexual arousal.

We appreciate your participation in this study! Feel free to contact us at the addresses below for any questions or concerns that you may have.

Phone: 512/232.4805
Quit.smoking.study@gmail.com

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